A.M.A.

American Journal of DISEASES OF CHILDREN

TREATMENT OF THYROTOXIC CHILDREN WITH THIOUREA DERIVATIVES
RALPH H. KUNSTADTER, M.D., ET AL.

NEONATAL TUBERCULOSIS
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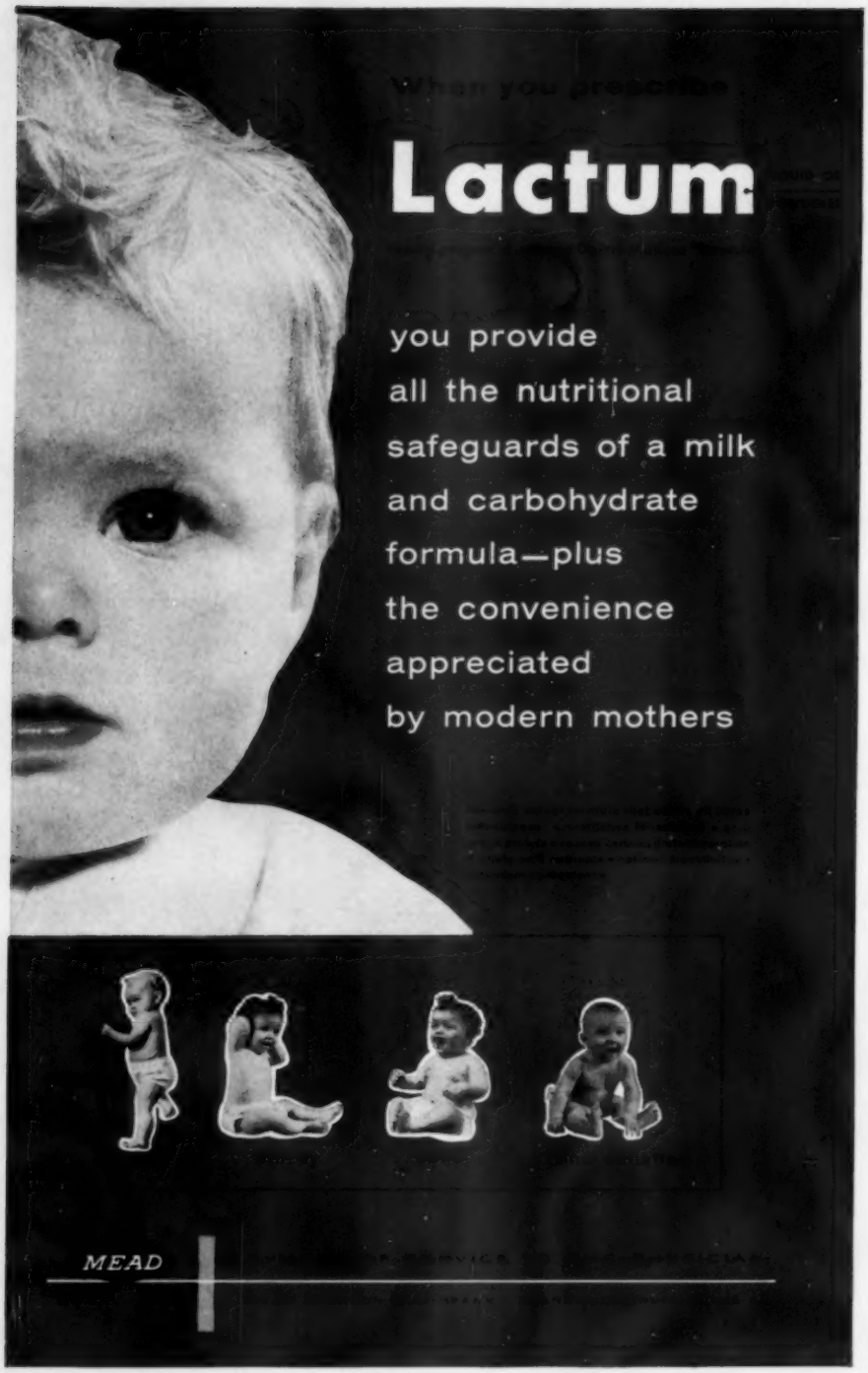
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American Journal of Diseases of Children

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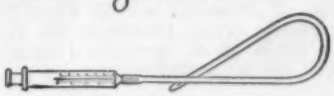

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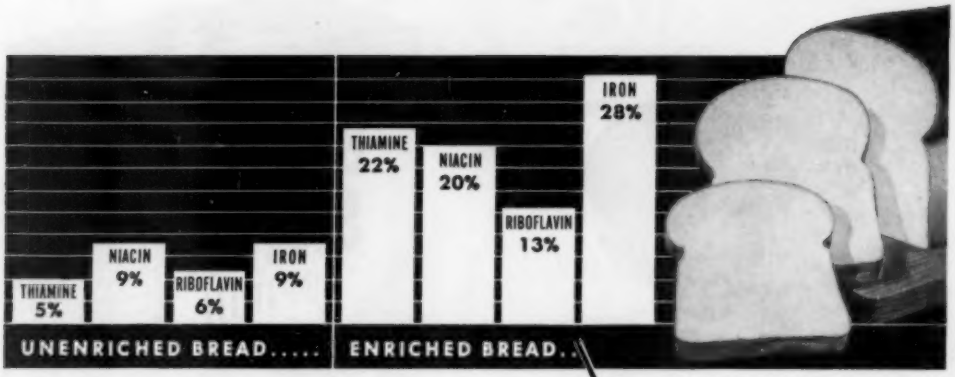

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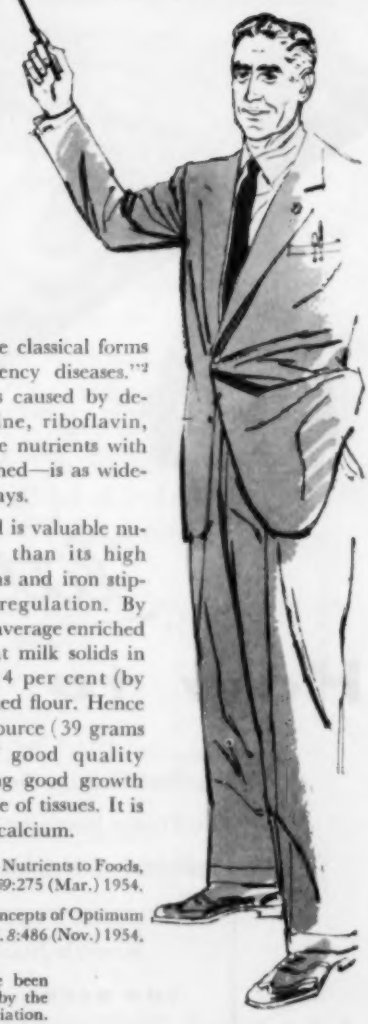

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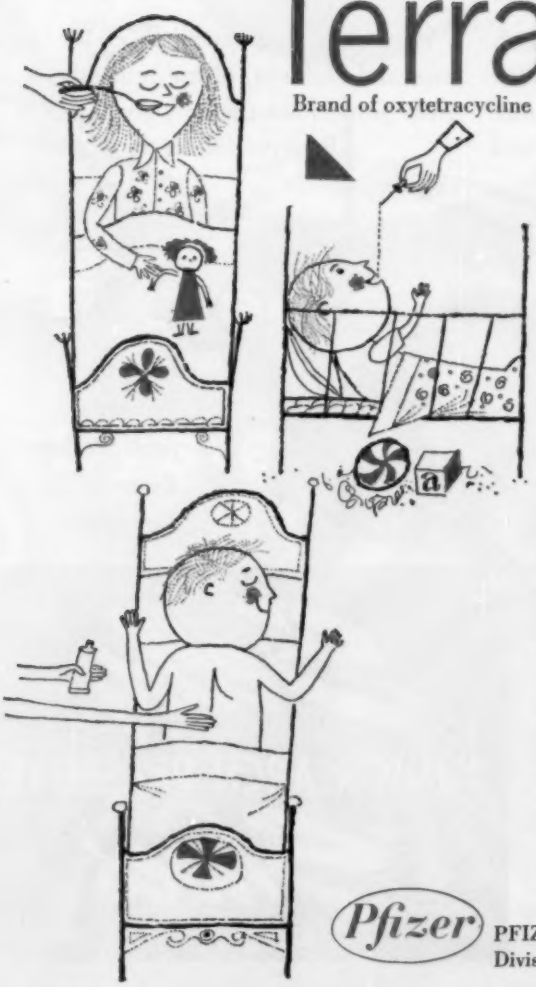

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*Farley, W. J.: Oxytetracycline in Pediatrics, Internat. Rec. Med. *168*:140 (March) 1955.

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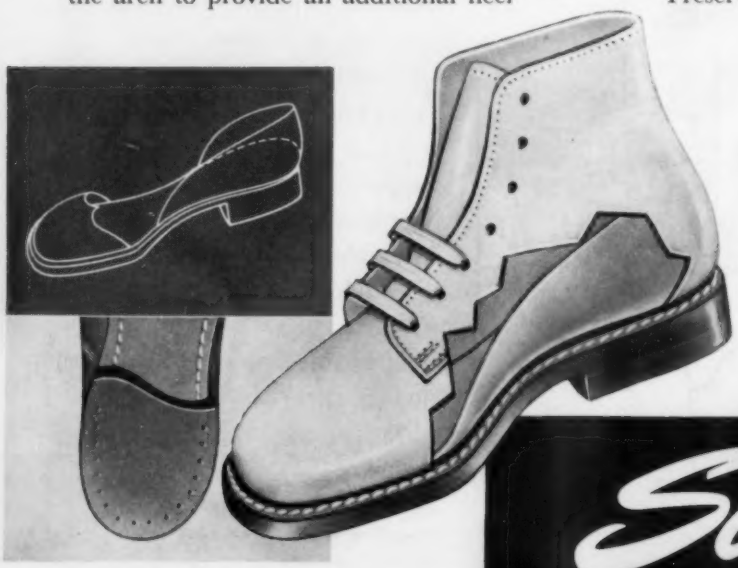

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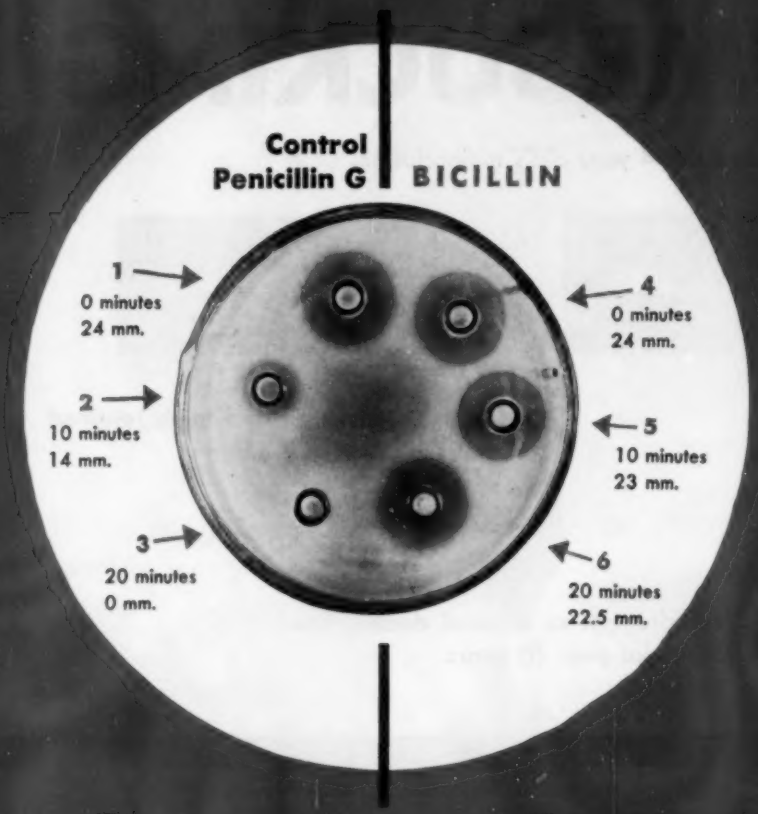

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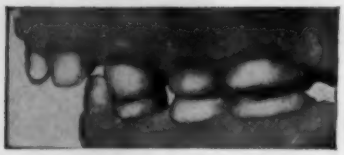

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1. Ratner, B. et al: A.M.A. Am. J. Dis. Child. 89:187, 1955.
2. Glaser, J., and Johnstone, D. E.: J.A.M.A. 153:620, 1953.

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Treatment of Thyrotoxic Children with Thiourea Derivatives

Long-Term Follow-Up and Recent Experiences

RALPH H. KUNSTADTER, M.D.
and
ALBERT F. STEIN, M.D., Chicago

In 1949 we reported our experience with thiourea derivatives in the treatment of nine children with hyperthyroidism due to diffuse toxic goiter and were impressed by the remissions obtained in five of these treated successfully.[1] Their ages were 9, 11, 9, 5, and 13½ years and they were treated continuously for 13, 12, 7, 15, and 6 months, respectively. Subtotal thyroidectomy was performed on four of the nine patients, for the following reasons: (1) marked enlargement of the thyroid, although the patient was euthyroid after five months of treatment *; (2) refractoriness to the drug during treatment following a third relapse; (3) slow response to the drug in a child who had psychotic episodes and cardiac complications, and (4) poor cooperation from a badly disturbed child. Thus, only one case can be considered a drug failure.

Because a great deal of controversy exists as to the advisability of prolonged treatment with thiourea drugs, we believe that a follow-up report on the original nine and our experience with eight additional patients since 1949 may answer some of the questions raised, namely: is permanent "cure" possible; what dose should be administered and how long should the drug be taken; what is the effect on growth and development; what happens to the size of the goiter and exophthalmos, and, finally, what are the advantages of prolonged medical treatment?

The original nine patients (including the four thyroidectomized) have been observed for periods ranging from 6½ to 12 years, and the additional 8 patients, from 4 months to 6 years.

Submitted for publication June 30, 1955.

From the Children's Endocrine Clinic and the Sarah Morris Hospital for Children.

* A surgical consultant insisted upon thyroidectomy, not realizing the early goitrogenic properties of thiourea drugs. This was our second patient, treated in 1943.

CLINICAL MATERIAL

During the past 12 years we have treated 17 cases of mild to severe primary hyperthyroidism in children with thiourea derivatives; the first two cases were treated with thiouracil, the third with thiouracil, propylthiouracil, and methylthiouracil, and one with methylthiouracil. Subsequently, six were treated with propylthiouracil; two, with methimazole (1-methyl-2-mercaptoimidazole) and propylthiouracil, respectively, and five, with methimazole.

There were 13 girls and 4 boys in this group, their ages varying from 5 to 15 years. Thirteen were white and four were Negro.

All patients were hospitalized at the time treatment was begun. They were ambulant and received sedation for sleep only when it was deemed necessary. They remained in the hospital until clinical improvement became manifest and/or the basal metabolic rate began to fall. They usually remained no longer than two to three weeks.

All had symptoms of thyrotoxicosis for periods of several weeks to several months. In all instances the thyroid was moderately to markedly enlarged

and of the diffuse type. All had mild to moderate exophthalmos. The initial basal metabolic rates varied from +32% to +51.9%, with 12 of the 17 cases having initial rates of over +40%. Several of the more recent cases had I^{131}-uptake determinations. On the basis of the severity of the symptoms, size of the thyroid, and degree of exophthalmos, 11 were classified severe, 5 as moderately severe, and 1 as mild (Table 1).

Thiouracil,† methylthiouracil, and propylthiouracil were administered in doses of from 150 to 300 mg. or more daily in three divided doses at eight-hour intervals when practical. Methimazole was administered in doses of 30 to 60 mg. daily. In general, the size of the dose depended upon the size of the child and the severity of the disease. The majority received the accepted adult dose of 200 to 300 mg. or more daily and in the case of methimazole, 20 to 30 mg. daily. After a normal basal metabolic level was attained, the dose was gradually reduced and a maintenance dose of 50 to 100 mg. of thiouracil, methylthiouracil, or propylthiouracil and 10 to 15 mg. of methimazole daily was prescribed for several months, depending upon the severity of the disease and rapidity of initial response.

During the administration of full therapeutic doses, and while the dose was being reduced, basal metabolic rates were taken at one- to two-week intervals. The latter were used as a guide in order to avoid relapses resulting from too rapid reduction of the dose, which occurred in two of the early cases.

Complete blood cell counts and urinalysis were done every one to two weeks during administration of full therapeutic doses and as often as necessary during maintenance therapy. The patients were observed closely for jaundice. Electrocardiograms were taken periodically on those patients who responded poorly to initial treatment and on all of those who relapsed.

In those cases where the thyroid failed to decrease in size and thyrotoxicosis was controlled for several months, thyroid U. S. P., 0.015 to 0.03 gm. daily, was prescribed. It was given either while the patient was receiving maintenance therapy or during the period of remission.

RESULTS

A detailed study of the initial nine cases with a description of individual management is given in our original report [1] and will not be repeated. Rather, a summary of our results, with emphasis on duration of remissions; growth and development, including sexual development; size of the thyroid, and degree of exophthalmos is presented.

Prolonged medical treatment of from 6 to 36 months resulted in remissions of five years or more in six patients and of two to five years in two patients. From our experience with these eight patients, we have reason to be optimistic that some of the remaining four, still under treatment and in remission less than two years up to the present time, can be expected to continue in remission indefinitely, even after all medications have been terminated. Puberty through adolescence progressed normally,

TABLE 1.—*Cases Treated with Thiourea Derivatives*

No.	Age, Yr.	Sex	Race	Duration of Symptoms	Goiter *	Exophthalmos †	Severity of Disease
1	9	F	W	3½ mo.	+++	++	Severe
2	12	M	W	2 mo.	+++	+	Severe
3	13	F	N	7 wk.	+++	++	Severe
4	15	F	W	4 mo.	+++	+	Severe
5	11	F	N	5 wk.	++	+	Moderate
6	9	F	W	5 mo.	++	+	Moderate
7	5	F	W Mex.	2 mo.	+++	++	Severe
8	13½	M	W	4 mo.	++	++	Moderate
9	10½	M	W	3 mo.	+++	++	Severe
10	10	F	W	8 mo.	+++	++	Severe
11	8	F	W	6 mo.	++	++	Moderate
12	8	F	N	5 mo.	+++	++	Severe
13	15	F	W	6 mo.	+	+	Mild
14	7	F	W	2 yr.	++	+++	Severe
15	8	M	W	3 mo.	++	+	Moderate
16	12	F	W	3 mo.	++	+	Severe
17	9½	F	N	1 mo.	+++	+++	Severe

* Graded 1 to 4 on the basis of degree of enlargement.
† Graded 1 to 4 on the basis of relative degree of exophthalmos.

† Thiouracil has not been used since 1945.

and growth and development was normal in all of the six patients followed from five to nine years. Their present ages range from 13½ to 22 years. Case 1 died at the age of 18 years of a fulminating acute bacterial endocarditis, having been in remission for nine years. Her goiter and exophthalmos had completely disappeared. Of the remaining five patients, four have no goiters and no exophthalmos; one has no goiter and only mild exophthalmos. Three of these six patients had from one to three relapses, but resumption of the drug and increase in the daily dose resulted in subsequent remissions (Table 2).

The two patients, Cases 13 and 10, in remission for four and one-half and two and one-half years, respectively, present ages 20 years and 16½ years, experienced normal puberty and adolescence, with normal growth and development. The former is married and seven months pregnant. She has no goiter and no exophthalmos. She had no relapses. The 16½-year-old has mild exophthalmos and no goiter. She had one relapse, apparently due to severe tonsillitis, and subsequently, during a remission, underwent a successful tonsillectomy. At present she is perfectly well and attends high school (Table 3).

Four patients are still under treatment (Table 4). Case 14, age 7 years, has been under treatment continuously for 2 years and has been in a remission for the past year, although she has been on maintenance therapy for the past 11 months. At 9 years of age pubertal changes are present, namely, breast development and pubic hair; growth has been normal; the thyroid is normal in size and consistency, and the patient has rather marked exophthalmos. The tonsils and adenoids are considerably enlarged, and tonsillectomy and adenoidectomy is planned in the near future. Case 15, age 8 years, and brother of Case 7, has been under treatment continuously for two years. He has been in a remission for over eight months, although he is still on maintenance therapy. Growth is normal, and he shows only slight exophthalmos and a small goiter. Case 12, age 8 years, has been under interrupted treatment for approximately three years. She has had three relapses during this time, due in all probability to (1) a severe upper respiratory infection, (2) emotional disturbance and discontinuation of therapy, (3) severe gastroenteritis. She attends school, is underweight, and frequently is disturbed by marital difficulties between her mother and father. Growth is normal, and pubertal changes are beginning to appear. She has moderate exophthalmos and a slightly enlarged, firm thyroid. Case 17, age 9 years, is euthyroid after four months of treatment on full therapeutic doses. Her initial response was dramatic, with disappearance of all signs and symptoms of thyrotoxicosis in less than two months after initiation of therapy. She still has moderate enlargement of her thyroid and mild exophthalmos. On the basis of her rapid initial response and the fact that she is a quiet, cooperative child free from disturbing environmental influences, we expect that she will remain in remission indefinitely.

One patient, Case 16, age 12 years, presented unusual complications and is presented in more detail.

CASE 16.—A 12-year-old girl had had symptoms of severe thyrotoxicosis consisting of extreme nervousnes, loss of weight, diarrhea, large diffuse goiter, and moderate exophthalmos for over three months. Her BMR was +45%; cholesterol, 60 mg. per 100 cc., and fasting blood sugar, 47 mg. per 100 cc. She was given methimazole, 10 mg. every eight hours, and in three months she was euthyroid, with a BMR of —10%. She had gained 25 lb. Methimazole was reduced to 20 mg. per 24 hours. She remained well; the dose was reduced to 10 mg. per 24 hours and was finally discontinued after five months. Three months later she felt well, and her first menstrual period had occurred at this time. Examination of the thyroid revealed a nodule in the left lobe, walnut-sized and firm. Because of the possibility of an adenoma and/or carcinoma, a surgical consultation was requested. She was taken to another hospital outside of Chicago, where it was agreed that surgical intervention was indicated. At the time of operation, her BMR was —17%; protein-bound iodine, 5.0γ per 100 cc., and serum cholesterol, 254 mg. per 100 cc. A subtotal thyroidectomy was performed. Histological diagnosis was "parenchymatous hypertrophy with associated lym-

TABLE 2.—*Remission Five Years or More*

Case	Present Age, Yr.	Age at Onset of Treatment, Yr.	Drug *	Duration of Treatment, Mo.	Relapses, No.	Probable Cause of Relapse	Duration of Remission, Yr.	Onset of Puberty	Growth and Development	Present Status
1.	18	9	T	13	3	A. Thyroid medication B. Shortage of drug C. Severe URI	9	13 yr.; first menstrual period 13 yr. of age	Normal	Died of acute bacterial endocarditis at 18 yr.
5.	18	11	P	12	0	.....	5	13½ yr.; first menstrual period 13½ yr. of age	Normal	No exophthalmos, no goiter
6.	15	9	P	7	1	Too rapid reduction of dose	6	12½ yr.; first menstrual period 12½ yr. of age	Normal	No exophthalmos, no goiter
7.	18½	5	P M	36	3	A. Severe URI B. Severe tonsillitis C. Severe tonsillitis (all while on maintenance doses)	5½	13 yr.; first menstrual period at 13 yr. of. age	Normal	Tonsillectomy during remission; mild exophthalmos, no goiter
8.	22	13½	P	6	0	.....	8	14 yr.	Normal; Ht. 72 in., Wt. 180 lb.	Graduated from college; no exophthalmos, no goiter
11.	14	8	P	9	0	.....	5	11¾ yr.; first menstrual period 11¾ yr. of age	Normal	High school; no exophthalmos, no goiter

* T, thiouracil; P, propylthiouracil; M, methimazole.

TABLE 3.—*Remission Two to Five Years*

Case	Present Age, Yr.	Age at Onset of Treatment, Yr.	Drug *	Duration of Treatment, Mo.	Relapses, No.	Probable Cause of Relapse	Duration of Remission, Yr.	Onset of Puberty	Growth and Development	Present Status
10.	16½	12	M	21	1	Severe tonsillitis	2½	11½ yr.; first menstrual period 11½ yr. of age	Normal	Tonsillectomy during remission; well at present, high school, mild exophthalmos, no goiter
13.	20	15	M	6	0	.....	4½	13 yr.; first menstrual period 13 yr. of age	Normal	Well, married, pregnant; no goiter; no exophthalmos

* M, methimazole.

TABLE 4.—*Patients Under Treatment*

Case	Present Age, Yr.	Age at Onset of Treatment, Yr.	Drug *	Duration of Treatment, Mo.	Relapses, No.	Probable Cause of Relapse	Duration of Remission	Onset of Puberty	Growth and Development	Present Status
14.	9½	7	M	24	0	.....	1 yr. (still on maintenance therapy)	9 yr.; breast development, pubic hair; no menstruation	Normal	Euthyroid, exophthalmos marked; goiter small, large tonsils and adenoids
15.	10	8	P	24	0	.....	8 mo. (still on maintenance therapy)	.....	Normal	Mild exophthalmos, small goiter, euthyroid; going to school
16.	13½	12	M	7½	0	.....	11 mo.; 5 mo. no treatment	13 yr.; first menstrual period 13 yr. of age	Sexual development normal, marked obesity, hypothyroid	Subtotal thyroidectomy for "tumor"; histologic diagnosis, thyroiditis; postoperative tetany, paralysis vocal cord, myxedema; at present, obese, hypothyroid, mild exophthalmos
12.	11	8	P	36	3	A. Severe URI B. Severe emotional disturbance C. Severe gastroenteritis	Euthyroid, still under treatment	Beginning pubertal changes	Growth normal, underweight	Moderate exophthalmos; slightly enlarged firm thyroid; still under treatment; emotional problems
17.	9½	9	M	6	0	.....	4 mo.; still under treatment	.....	Normal	Remission for 4 mo.; still under treatment

* T, thiouracil; P, propylthiouracil; M, methimazole.

phocytic thyroiditis and areas of regenerative hyperplasia." Twenty-four hours postoperatively she developed hypocalcemic tetany, with serum calcium 7.5 mg. per 100 cc. and phosphorus 4.0 mg. per 100 cc. There was a paralysis of the left vocal cord. With dihydrotachysterol (A. T. 10) and calcium she recovered from the tetany, and she was discharged from the hospital 14 days postoperatively on dihydrotachysterol, calcium, and strong iodine solution U. S. P. (Lugol's solution). When we saw her on the 16th postoperative day she appeared bloated and pale and had gained 12 lb. during this time. She appeared myxedematous. She had no further tetany, and she had recovered from vocal cord paralysis. During the following two months she gained another 17 lb. She had not menstruated since her operation. At this time her BMR was —43%; protein-bound iodine was 4.6γ per 100 cc.; calcium, 9.6 mg. per 100 cc., and phosphorus, 5.2 mg. per 100 cc. Dihydrotachysterol and strong iodine solution U. S. P. were discontinued, and she was given 1.5 grains (90 mg.) of desiccated thyroid daily. Thyroid was gradually increased to 2.5 grains (150 mg.), and during the following two months she improved remarkably; menstruation occurred, myxedema disappeared, her weight dropped 10 lb., and she no longer felt sluggish. Her BMR had risen to —2%. She is still receiving calcium and thyroid.

The present status of the five patients submitted to subtotal thyroidectomy is shown in Table 5.

TABLE 5.—*Patients Thyroidectomized After Medical Treatment*

No.	Sex	Age at Onset of Treatment, Yr.	Duration of Medical Treatment, Mo.	Reason for Thyroidectomy	Age at Time of Thyroidectomy, Yr.	Present Age, Yr.	Present Status
2.	M	12	5	Marked thyroid enlargement	12½	21	Retarded growth
3.*	F	13	26	Refractoriness to drugs	15½	19	Recovered from hypothyroidism
4.	F	15	6	Slow response to drug; psychotic episodes; cardiac complications	15½	20	Normal
9.	M	10½	3	Poor cooperation	10¾	16	Recovered from hypothyroidism, marked obesity, severe keloid scar
16.	F	12	7½	Nodule in thyroid	12¾	14	Hypothyroid, obesity

* Case 3. Classified severe. R. F., a Negro girl, 13 years of age, was treated for a total of 26 months. She received thiouracil for 6 months, propylthiouracil for 18 months, and, following a relapse after a 5½ month remission, methylthiouracil for two months. BMR fell slowly and did not reach normal until after 180 consecutive days of thiouracil and 91 days of propylthiouracil—a total of 271 days. Initially she received thiouracil, 300 mg. daily for 16 days, 250 mg. for 10 days, and 200 mg. for 5 months. She was then given propylthiouracil, 250 mg. daily for 28 days, 200 mg. for 28 days, 250 mg. for 26 days, and 100 mg. for 2 months. At this time she developed a severe acute upper respiratory infection followed by a mild relapse. The dose was then increased to 200 mg. daily for 30 days, followed by 100 mg. for 3½ months and 50 mg. for 2 months. A second, severer relapse occurred at this time, apparently due to emotional shock when her father was killed. The dose was then increased to 300 mg. daily for 30 days followed by 100 mg. daily for 2 months and finally 50 mg. for 3½ months. Without treatment she experienced a remission for the following 5½ months. Subsequently, a third and severe relapse occurred for no obvious reason. She was then given methylthiouracil, 300 mg. daily for 21 days, 400 mg. for 25 days, and, finally, 600 mg. for 10 days. In spite of the large doses thyrotoxicosis persisted. Furthermore, the thyroid had increased in size. Methylthiouracil was discontinued, and she was given strong iodine solution U.S.P. for two weeks, at the end of which time a subtotal thyroidectomy was performed.

COMMENT

Prolonged medical treatment of thyrotoxicosis in children appears justified in view of prolonged remissions obtained in a good number of our patients treated; 6 of 17, or 35.5%, in remission for more than five years and 2 of 17, or 11.8%, in remission for two to five years. Since 4 of these 17 patients are still under treatment and responding satisfactorily, these figures eventually may be higher. Iverson [2] reported 144 cases of thyrotoxicosis treated with methylthiouracil which had been followed for an average of three years with a remission rate of 79.5%. Greenberg and Bruger [3] found a remission rate of 64% for longer than one year in 39 patients with toxic diffuse goiter treated with thiouracil and propylthiouracil. Beierwaltes and Sturgis [4] reported a remission rate of an average duration of 17 months in 86% of 35 patients with diffuse toxic goiter. Rose and Shorey [5] reported that 82.6% experienced a remission of one year or longer (38 of 46 patients). Sixty-nine per cent of these had sustained remission without preliminary relapses. McCullagh and Cassidy [6] treated 60 patients with thyrotoxicosis who had

small- to moderate-sized diffuse goiters with propylthiouracil. Forty patients, or 66.7%, remained in remission after discontinuing treatment for four or more years previous to this study. On the basis of an analysis of all these figures and our own, prolonged remissions, of at least four years, or longer, may be anticipated in from 45% to 65% or slightly more of patients treated with thiourea derivatives over a long period of time.

From our own experience and that of others,[6] we believe that the longer treatment is continued the more likely is the chance of permanent remission. None of our patients were treated for less than 6 months, and the range varied from 6 to 36 months for those who have completed treatment. The average duration of treatment was 13.75 months. The severe cases with large goiters required larger doses and more prolonged treatment than those of less severity with smaller goiters. As we have emphasized previously,[1] children tolerate large doses, and in most cases those over 8 years of age were able to take adult doses. In our small series, no toxic manifestations were observed in any of our patients. Bartels and his coworker,[7] in treating some 2000 hyperthyroid patients with propylthiouracil, found that the incidence of reactions was only 1.5% and that the reactions did not seem to be related to the size of the dose. In 24 adult patients, Bartels administered from 600 to 1000 mg. daily of propylthiouracil and found that these doses could be used with comparative safety.[7] Not only is the initial response more rapid with large doses but we also believe that relapses are less likely to occur and that the length of treatment may be shortened.

As a result of being able to follow a number of our patients in remission for long periods, it was possible for us to observe the effects of treatment on growth and development, including sexual maturation. It has been gratifying to us that in all of the six patients in remission for more than five years and in the two in remission for two to five years these processes have progressed normally. Also, encouraging are the facts that the goiters have disappeared in all of these eight patients and only mild exophthalmos remains in two.

Subtotal thyroidectomy for thyrotoxicosis is still considered the treatment of choice in many clinics, primarily because of the high rate of recurrence following medical therapy and the reluctance of many patients to carry out prolonged treatment.[8] Nevertheless, in spite of the fact that cure of thyrotoxicosis with thiourea derivatives may be unpredictable, there are problems and circumstances incident to childhood which justify prolonged medical treatment of thyrotoxicosis in most instances. Even in the hands of skillful surgeons the possibility of recurrences[9] and postoperative effects on growth and endocrine function is real (Table 5). As Topper[10] states, "the question of the amount of thyroid tissue to be removed is always problematic, since future demands on the gland are unpredictable." Furthermore, endocrine balance is more easily disturbed in childhood and may be difficult to control with endocrine therapy. During the past several years we have had under our care five thyroidectomized children (not included in the present study) who developed postoperative endocrine disturbances: retarded growth, hypoparathyroidism, hypothyroidism, and polyglandular disturbances, including retarded sexual development and obesity. Because of the possibility of such disturbances, it is believed that thyroidectomy should be avoided if possible.

As Williams[11] recently stated, treatment with thiourea derivatives is relatively simple and inexpensive and is not associated with paralysis of vocal cords, hypoparathyroidism, or permanent myxedema. He also stated that subtotal thyroidectomy is the treatment of choice primarily when a large nodular gland is present or when a rapid recovery is one of the main objectives. We agree that persons with small goiters and those with mild thyrotoxicosis have the best opportunity for permanent remission.

Prolonged medical treatment in children usually does not impart the economic hardships that it does with adults, who may have to take time away from their jobs and thus jeopardize their livelihoods. The problems of prolonged follow-up, with frequent visits to the physician, usually offer no difficulty. Parents and patients are usually cooperative.

SUMMARY AND CONCLUSIONS

During the past 12 years we have treated 17 cases of mild to severe primary hyperthyroidism in children with thiourea derivatives. Five were submitted to subtotal thyroidectomy: only one because of drug failure, the others for the following reasons: (1) marked enlargement of the thyroid, (2) psychotic episodes and cardiac complications during early treatment, (3) poor cooperation from a badly disturbed child, and (4) development of a nodule in the thyroid suspected of being a neoplasm. Twelve patients have been followed under medical treatment alone. Of these, six have been in remission for five years or more; two have been in remission for two to five years, and four are still under treatment.

Prolonged treatment of from 6 to 36 months was administered to the eight patients in remission. These children tolerated large doses, in most instances full adult doses, without evidence of toxicity. We believe that initial large doses result in earlier response, lessen the likelihood of early relapses, and may shorten the duration of treatment.

In all the patients followed in remission for long periods of time, growth and development, including sexual maturation, progressed normally through puberty into adulthood.

On the basis of our observations in this relatively small number of cases, we believe that attempts at prolonged treatment with thiourea derivatives are justified for the following reasons:

1. "Cures" of five years or more can be anticipated in a large percentage of patients.

2. Growth and development, including sexual maturation, progress normally during treatment and subsequent prolonged remission.

3. The possible complications of surgery and the sequelae of disturbed endocrine balance resulting from thyroidectomy may be avoided.

Dr. Joseph K. Calvin gave permission to report Case 14, and Dr. Julius H. Hess collaborated in the management of Case 16.

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Neonatal Tuberculosis

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While the prognosis of tuberculosis in children generally has improved since the introduction of specific drugs, there has not been a progressive improvement in the outlook for the youngest age group. This lag may be due in part to inadequate defense mechanisms and immature physiologic responses. It may be hoped, however, that better results can be obtained if the peculiarities of the disease in very young infants are appreciated and diagnostic and therapeutic standards are chosen accordingly. For this reason we present observations on five consecutive cases of neonatal tuberculosis, with emphasis on autopsy findings.

All the patients are believed to have acquired their infection by aspiration either at birth or within a few days thereafter. Four were premature infants, one was born at term. One case occurred before the drugs currently used in the therapy of tuberculosis were available. In the remaining cases some sort of specific therapy was used. Although the five cases have certain features in common, there was a fairly wide range of manifestations and pathologic findings.

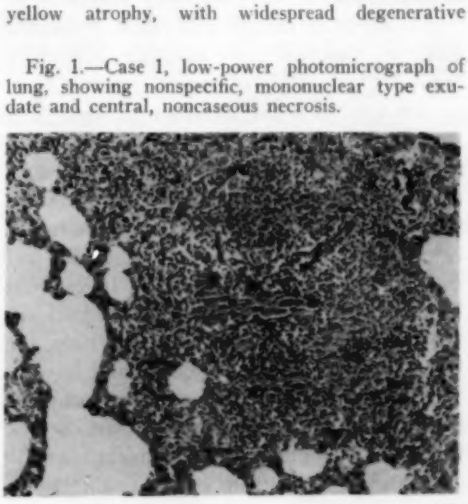
CASE 1.—R. H., a premature Negro boy, reported to have weighed 2½ lb. at birth, had seemed to do well until three days prior to admission, when he had fever, cough, vomiting, and abdominal distention. He shortly became jaundiced and was admitted, at the age of 7 weeks, in a moribund state. He weighed 4 lb. 15 oz., but appeared malnourished. There was icterus of sclerae and skin. Liver and spleen were significantly enlarged. The heart rate was slow and the sounds of poor quality. Breath sounds were faint over both lung fields. The abdomen was distended. The patient died within 15 minutes after admission.

The autopsy, performed without indications for the presence of tuberculosis, disclosed multiple pale yellowish abscess-like lesions disseminated over the peritoneal surfaces, throughout the liver, spleen, kidneys, adrenals, the walls of the alimentary tract, and the lungs. In the lingula of the left upper lobe two or three large, confluent, firm, yellowish lesions were found surrounded by satellite lesions extending in a fan-like spread toward the hilum. The hilar and paratracheal lymph nodes were enlarged, fluctuant, and on sectioning filled with yellow necrotic material. A poorly localized area of softening was present in each of the occipital lobes of the brain.

On the basis of the gross findings the impression at the time of the autopsy was that of a fulminating pyogenic infection. Even the histologic diagnosis was not immediately apparent. The areas corresponding to the gross lesions were areas of necrosis with more or less complete obliteration of the original tissue structure but without tubercle formation, giant-cell response, or other indications as to the true nature of the process. In the lungs the lesions were usually discrete and composed of an exudate consisting almost entirely of mononuclear cells (Fig. 1). Throughout, enormous numbers of typical acid-fast bacilli were demonstrable.

The liver presented a picture resembling acute yellow atrophy, with widespread degenerative

Fig. 1.—Case 1, low-power photomicrograph of lung, showing nonspecific, mononuclear type exudate and central, noncaseous necrosis.



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Children's Hospital of Michigan and Wayne University College of Medicine, Detroit.

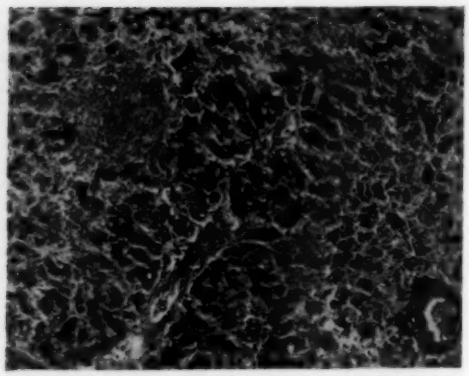


Fig. 2.—Case 1, photomicrograph of liver, showing disruption of architecture and area of necrosis (lower right).

changes throughout the parenchyma. In addition there were innumerable discrete foci of necrosis similar to those found in the lung and likewise containing many acid-fast bacilli (Fig. 2). The spleen was hemorrhagic, and here, as in the bone marrow, kidneys, adrenals, alimentary tract, meninges, spinal cord, and skin, necrotic lesions were found in abundance.

Comment.—This case of tuberculosis in a premature infant was characterized by a short clinical course resembling that of an overwhelming pyogenic infection. The autopsy findings indicated a virtually complete lack of the usual tissue response and an unchecked multiplication and spread of the tubercle bacilli, suggesting that the necrosis found in nearly every organ was the direct result of the presence of enormous numbers of organisms in an anergic individual. Repeated massive exposure to infection therefore seemed likely. It is of special interest that, on the contrary, the evidence pointed to a single, chance exposure. It will be recalled that the patient was one of twins. The other twin was healthy and when last examined, at the age of 9 months, had a negative tuberculin reaction and a normal chest film and was gaining well. The mother, a 16-year-old Negro girl, had no evidence of tuberculosis. No other contacts were found within the family or among the neighbors and friends. It was learned that many visitors had come to see the twins in the first few weeks. The twins had occupied the same basket but with their heads facing in opposite directions. This fact may explain the occurrence of the tuberculous infection in only one of the twins and suggests that single exposure from a source outside the household caused the disease. Under these circumstances the course and the unusual histologic picture indicate virtually complete absence of defensive mechanisms in this premature infant.

Case 2.—K. W. was admitted one-half hour after birth, following a 6½-month gestation. Delivery had been preceded by three days of cramps and vaginal bleeding. The parents and three siblings were thought to be in good health, and there was no history suggestive of tuberculosis.

Admission weight was 2 lb. 10 oz. There were no apparent abnormalities. Laboratory findings were within normal limits. He was placed in the premature nursery, where his course during the first three weeks was not unusual except for a continuous lability of temperature, which occasionally spiked slightly above normal. Three weeks after his admission his mother was found to have miliary tuberculosis. Roentgenograms of the infant's chest at this time revealed extensive infiltrations in the right upper lung field and in the medial basal area of the right lower lobe. Only a few scattered rales were heard, but he was described as lethargic. Tuberculin skin tests were negative in dilutions of 1:1000 throughout his life. Spinal fluid obtained at this time and on subsequent occasions was negative except for an elevation of the protein, which fluctuated between values of 69-189 mg. per 100 cc. All cultures of spinal fluid and three gastric washings were negative for tubercle bacilli.

At 4 weeks of age therapy with 150 mg. of streptomycin and 0.6 gm. of paraaminosalicylic acid (in divided doses) daily, was started. Three weeks later the dose of streptomycin was increased to 250 mg., at which time the infant weighed 4½ lb. Paraaminosalicylic acid was discontinued for slightly more than a month because of a protracted period of diarrhea from which he eventually recovered. His weight reached 6 lb. for a short while but began a slow decline a few weeks prior to death. His temperature continued to fluctuate between normal and subnormal levels, with occasional elevations to 100 or 101 F. Persistent temperature elevation gradually developed prior to death. By 4 months of age the right lung was extensively consolidated, and a large cavity appeared in the left upper lung field together with an area of consolidation in the left lower lung field. Early in the course of his disease he developed an extensive periostitis of his right humerus. Multiple rib fractures were also observed, but were thought to be secondary to violent coughing rather

than to tuberculous osteitis. Both the humeral and the costal lesions showed signs of healing by 4 months of age, but at that time gastric washings showed enormous numbers of acid-fast rods on direct smear. A thick nasal exudate and a distressing paroxysmal cough appeared. Whole-blood transfusions, other antibiotics, and supplementary nutriments were included in his management. In spite of continuous therapeutic effort he died at 5½ months of age.

At autopsy the body was cachectic. Both lungs were firmly bound to the lateral chest wall by fibrous adhesions. Large, and frequently caseous, lymph nodes circumscribed the trachea and mediastinum. Only the right middle and lower lobes appeared to contain any aerated lung, the remaining parenchyma being completely replaced by soft nodular, and confluent masses; many small discrete nodules were present in the right lower lung fields. The main-stem bronchi on the left entered into a large ragged excavation in the left upper lobe and into a smaller smoothly lined cavity in the apex of the left lower lobe. Several discrete firm nodules were present in the spleen.

Sections of lung showed few recognizable alveoli. There were numerous, irregularly distributed, small fibrous tubercles, usually free of giant cells, often containing small centers of caseation. These, in many instances, were situated in close approximation to blood vessels. The greatest portion of the lung was infiltrated by an extensive pneumonic exudate of mononuclear cells, which filled the alveoli and left only ill-defined remnants of the alveolar septa. Many of these areas were caseous and excavated so that several small cavities with walls formed by pneumonic lung were seen. Enormous numbers of acid-fast organisms were found. Giant cells and tubercle formation were almost completely absent in the pneumonic areas. The little recognizable lung that remained was uniformly altered by interstitial inflammatory changes consisting usually of fibroplasia and cuboidal metaplasia of the remaining epithelium. The spleen contained many small fibrous miliary tubercles that were relatively free of lymphocytes, caseation, or giant cells. In addition, there was extensive hemosiderosis and erythrophagocytosis, probably secondary to the many transfusions given. In several tubercles a small amount of fibrin-like material was present in the center. The more cellular tubercles contained a few acid-fast rods. Similar tubercles were scattered throughout the liver, where there was moderate dissociation of the cell cords and where many of the liver cells were large and binucleate, some containing as many as four or five nuclei. Giant cells were present but not ubiquitous. Hemosiderosis was also extensive here. No bile-duct proliferation was seen.

Comment.—This premature infant was most likely infected at the time of birth. There was no evidence of a hepatic primary complex to indicate prenatal, placental infection. Although the disease was well established at 3 weeks of age, there had been practically no clinical evidence to arouse suspicion. An unremitting progressive infection occurred, and, despite therapy, there was little anatomic evidence of healing in the autopsy studies. The clinical course and anatomic findings are characterized by a minimal defensive response by the patient. No evidence of tuberculin sensitivity developed during the five and one-half months of his life. In addition to disseminated miliary lesions, the significant finding was extensive tuberculous pneumonia. This case is quite similar to Case 1 in severity and its lack of ability to alter the progression of infection. Prolongation of life occurred because of an early awareness of the possibility of infection and the use of specific antibiotics.

CASE 3.—A. S. was a prematurely born Negro boy. Details of the mother's pregnancy were not available, but social conditions were known to have been poor. Birth occurred in an ambulance, and the placenta was discarded. When admitted to another hospital the infant weighed 3 lb. 12 oz. Shortly after admission the mother was found to have miliary tuberculosis and was separated from the child. He did well, under good routine care, until 7 weeks of age, when he became listless and dyspneic. Slight cyanosis was present, and diffuse rales were heard throughout both lungs. Chest films revealed a dense shadow in the area of the right upper lobe and a smaller area of infiltration near the left cardiac border in the left midlung field. No lymph-node enlargement was present. Treatment with antibiotics and transfusion failed to produce any clinical response, and he was therefore transferred to our hospital a few days after the onset of symptoms.

He did not seem severely ill, and his nutritional state was good. He weighed 5 lb. 1½ oz. His temperature was 99.8 F. The respirations averaged 50/min. Dullness and decreased breath sounds were present over the area of the right upper lobe. Many fine sticky rales, and occasional coarse rales, were heard over the left chest. Hemoglobin was 11.6 gm. per 100 cc., WBC 18,000 per cubic millimeter, with a slight shift to the left. Results of urine and Mazzini tests were negative. The Mantoux test was questionably positive in a dilution of 1:1000,

but definite at 1 : 500. The spinal fluid was negative on two occasions, and no tubercle bacilli were cultured. Gastric washings, however, produced acid-fast organisms on culture.

Treatment with 1 gm. of streptomycin daily (approximately 200 mg/lb/day) and 1.75 gm. of thiazolsulfone (Promizole) four times daily was begun one week after admission. Throughout the first two weeks the temperature was quite labile, and for the rest of his life there was a persistent elevation, with temperatures ranging between 101 and 102 F. Nevertheless, he gained weight slowly, until he weighed 6 lb. at 10 weeks of age, when growth ceased. Hemoglobin values tended to fall rapidly but were maintained by frequent transfusions of whole blood. He had one severe episode of respiratory distress due to his inability to expel secretions. He usually ate well, but there were increasingly frequent periods of listlessness, when it was necessary to feed by gavage. For a short period his urine contained albumin, occasional red cells, and granular casts. Roentgenograms of the chest taken at frequent intervals showed slight increase in the density of the lesions, with some slight spread, but the general appearance remained essentially unchanged except for progressive development of emphysema in the right lower and left upper lung fields. The mediastinal nodes did not seem enlarged at any time. During his last two weeks of life he became increasingly listless and deteriorated rapidly. He was found dead, lying in a pool of vomitus, at 3 months of age.

At autopsy, only the right middle lobe was found to be well aerated. The right upper and lower lobes were extensively consolidated or nodular. Most of the left lower lobe and the inferior portion of the left upper lobe were replaced by a massive caseous pneumonia, while the left apex was riddled with more discrete nodular lesions. The right upper lobe was destroyed by widespread caseation and fibrosis. Numerous caseous nodules extended laterally from the hilum to involve most of the right lower lobe. The liver and spleen were enlarged and also contained numerous nodular lesions.

Microscopically, most of the lung was found to be involved with an extensive tuberculous pneumonia, with wide areas of necrosis and intervening groups of confluent tubercles. Many of the more discrete lesions, especially those in the left upper lobe, showed definite fibrosis. All of the mediastinal and cervical nodes studied showed severe involvement. Acid-fast organisms could be found with ease in the necrotic areas.

Discrete fibrotic tubercles were found in the liver and spleen, with very few giant cells and very little vascularization. Several changes were seen in the kidneys, where there was wide separation of the tubules by edema and varying degenerative changes in the tubular and cortical epithelium. The interstices were widely infiltrated with numerous small lesions composed of lymphocytes, macrophages, and dilated capillaries. In some such lesions giant cells were found. Particularly noticeable were moderate numbers of eosinophiles in most of the lesions. A lower number of small, more typical, epitheloid tubercles were present. A small fibrous tubercle was present in one of the marrow sections. A few small perivascular infiltrations of lymphocytes were present in sections of the heart, which also showed a distinct edema of the myocardium.

Comment.—The presence of tuberculin sensitivity at 7 weeks of age and the discovery of disease in the mother at the time of delivery indicate that infection was acquired at approximately the time of birth. There was no evidence of a hepatic primary complex to indicate placental transmission of the infection. Infection by aspiration may have occurred either during delivery or by contact with the mother immediately postpartem. Death was due to progressive tuberculous infection. Although treatment was delayed until the infection was sufficiently well established to produce symptoms, there was, nevertheless, some evidence of healing in the microscopic sections.

Case 4.—G. M. was admitted at the age of 2 months because of difficulty in breathing during the previous three days. He was a full-term Negro infant and had seemed well until the onset of symptoms. His father subsequently was admitted to another hospital with far-advanced tuberculosis.

The infant was well nourished but appeared to be in moderate respiratory distress and perspired easily. The breath sounds were distant, and occasional rhonchi were audible over both lungs, but there were no localizing signs.

A mild anemia was present and the white blood cell count was 17,200 per cubic millimeter. Urinalysis was consistently negative. The spinal fluid contained 106 mg. per 100 cc. of protein but was otherwise negative. Two weeks later the spinal fluid protein was 57 mg. per 100 cc. and the other studies were negative. Smears of gastric washings were negative for tubercle bacilli. An x-ray of the chest showed severe hilar and interstitial infiltration, with narrowing of the trachea in the thoracic portion. The Mantoux test was found to be positive in a dilution of 1 : 1000 on the 10th hospital day, at which time streptomycin therapy, in a dose of 400 mg. daily, was begun. Thiazolsulfone therapy,

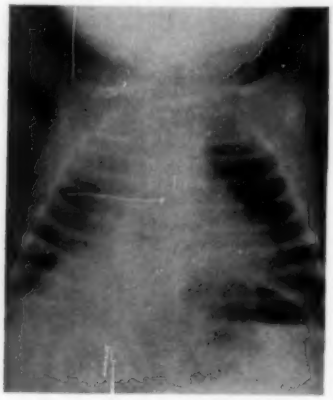
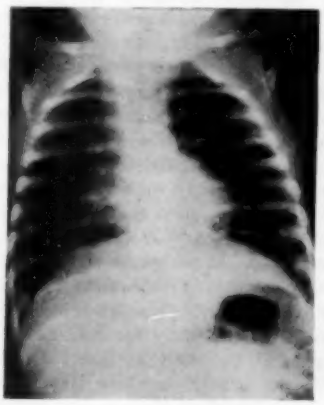


Fig. 3.—Case 4, first chest film, March 28, 1950. Consolidation of right apex and base, with diffuse bilateral miliary lesions.

in a dose of 400 mg. daily, was begun later but had to be discontinued after 12 days of therapy because of toxicity.

Before the tuberculin test was found to be positive the patient was treated for bronchiolitis, but he responded poorly and needed oxygen much of the time. Laryngoscopy, performed because of wheezing and dyspnea, revealed edema of the false cords and arytenoids. Roentgenograms taken shortly after admission showed a faint miliary process in both lungs. A dense area of consolidation in the right upper lung field cleared rapidly but was soon replaced by a similar area in the right lower and midlung fields (Fig. 3). As time progressed this area became smaller and more sharply defined, while moderate lymph-node enlargement became visible in the right upper mediastinum two and one-half weeks after admission. Tracheal narrowing became progressively less apparent, but there were no further significant changes seen until the day before death, when an x-ray showed the lung fields to be more voluminous but the miliary lesions and the area of consolidation in the right lung seemed to have completely cleared (Fig. 4). Thiazolsulfone therapy was instituted on the 25th hospital day. Two days later the patient became febrile, began to vomit and to loose weight, and had an occasional loose stool. About a week later icterus appeared, the liver enlarged, and bile appeared in the urine, while the fever persisted. Thiazolsulfone therapy was discontinued after 12 days. The baby remained icteric and febrile, gradually weakened, and finally died at 4 months of age.

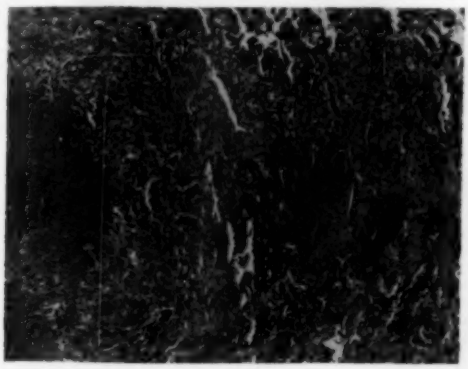
Fig. 4.—Case 4, May 20, 1950, taken day before death and showing generalized emphysema, with apparent resolution of initial lesions.



On postmortem examination the lungs were seen to be emphysematous, and small firm tubercles were scattered uniformly throughout both lungs. Large, caseous, and confluent nodes were found around the right main-stem bronchus and the carina and extending cephalad along the trachea. The primary lesion consisted of a large caseous focus in the apex of the right lower lobe, which was encircled by numerous smaller satellite lesions that extended toward the hilum.

The normal microscopic architecture of the lung in the area of the primary lesion was replaced by many caseating and frequently confluent tubercles of varying sizes. Most of the alveoli were atelectatic and distorted by extensive interstitial fibrosis, mononuclear cell infiltration, and cuboidal metaplasia of the remaining alveolar epithelium. Centrally, many of the tubercles were larger, and only here were a few acid-fast organisms demonstrated. Elsewhere in the parenchyma were scattered tubercles of uniform size and appearance, associated with adjacent zones of emphysema. All lesions, including the site of the primary infection, showed evidence of healing, the smaller ones in particular being fibrotic, hyalinized, and often partially vascularized (Fig. 5). Many of the hilar nodes

Fig. 5.—Case 4, photomicrograph of parenchymal fibrosis and fibrocaseous tubercle in lung.



showed evidence of healing. In the spleen, liver, and bone marrow there were numerous small fibrotic lesions that, individually, were often not diagnostic. A few small wedge-shaped foci were seen in the renal cortex and consisted chiefly of mononuclear-cell infiltration, capillary engorgement, and obliteration of the involved parenchyma. Giant cells and caseation were entirely absent in the extrathoracic lesions. The liver was involved only by a severe steatosis. No lesions were found in the central nervous system.

Comment.—This full-term Negro infant had an acquired, generalized tuberculosis presenting the clinical picture of an acute bronchiolitis. Tuberculin sensitivity was demonstrable on admission to the hospital, at 2 months of age. Following the institution of streptomycin and thiazolsulfone therapy there was an excellent roentgenologic response. His death, in the face of clearing x-rays and histologically healing lesions, apparently resulted from the effects of thiazolsulfone toxicity.

CASE 5.—T. W. was born unattended at home after an estimated 6½ months of otherwise uneventful gestation. On admission, at 3 hours of age, his weight was 2 lb. 14 oz. Admission physical examination and laboratory studies disclosed no abnormalities. He was placed on the premature ward and, except for the appearance of an inguinal hernia, he seemed to do well, gaining weight regularly after the first 10 days. The temperature was first subnormal, then labile, but appeared to stabilize after a few days. There were, however, irregularly occurring low-grade temperature elevations best seen in retrospect. He gained steadily,

Fig. 6.—Case 5, initial chest x-ray taken March 12, 1952. Diffuse bilateral miliary lesions, with large hilar lymph nodes.

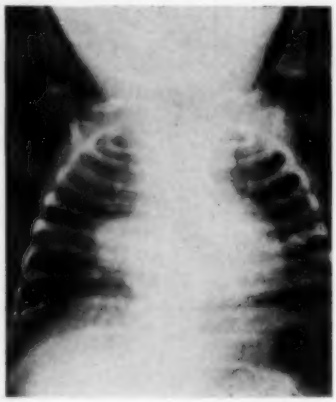


Fig. 7.—Case 5, x-ray June 2, 1952, showing clearing lung fields, well-defined hilar lymph nodes, and early emphysema.

weighing 5½ lb. at the end of two months. Occasional mild upper-respiratory-tract infections were handled easily with only penicillin and supportive therapy. At 2 months of age, however, he developed a chronic, yellow, nasal discharge and a barking, nonproductive cough which did not respond to treatment. At this time it was first learned that the mother had died of tuberculosis, and a chest film was taken for the first time, revealing a generalized miliary pattern with nodular masses in the left hilum (Fig. 6). Both the liver and the spleen were enlarged. Tuberculin tests were negative up through 1:100.

Streptomycin therapy was started and maintained at a daily dose of approximately 70 mg/lb. in conjunction with paraaminosalicylic acid at a dose of 0.1 gm/lb/day. Six months later streptomycin was reduced to a dose of 40 mg/lb three times weekly. During this initial period of treatment there was first progression of the pulmonary lesions and enlargement of the hilar nodes, then a gradual resolution began (Fig. 7). The Mantoux test was repeated at intervals of two or three weeks with dilutions of 1:1,000 and 1:100 but remained negative. Repeated gastric washings failed to give growth of tubercle bacilli. Following the clinical diagnosis of tuberculosis periodic lumbar punctures were done. The total protein values were elevated initially, but the other findings were not sufficiently abnormal to warrant action. About one month after onset of therapy, however, there were 36 lymphocytes in the spinal fluid and a total protein value of 100 mg. per 100 cc. (which was about as it had been), but the sugar was normal. These findings were taken as indication for intrathecal streptomycin therapy. This was accordingly begun in doses of 15 mg. daily for nine days, then increasing to 25 mg. daily for one week, following which 25 mg. was given three times weekly for

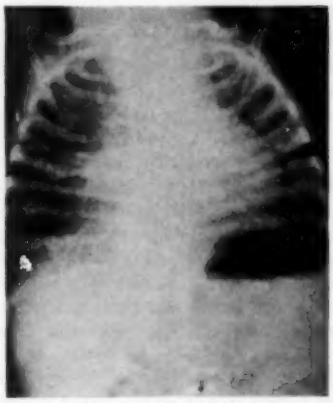


Fig. 8.—Case 5, Sept. 3, 1952. X-ray taken at time tuberculin skin sensitivity first appeared, showing reappearance of diffuse, "soft," miliary lesions. These cleared rapidly.

three weeks. During this period there was no significant change in spinal-fluid findings, but there were slight elevations of the over-all temperature, associated with small spikes following administration of intrathecal streptomycin. This procedure was therefore discontinued for two weeks for re-evaluation, but no appreciable change was noted. Intrathecal streptomycin was resumed in a dose of 25 mg. three times weekly for a second period of nearly five weeks. A marked variability of spinal-fluid findings characterized the whole course, but the total protein ranged between 60 to 120 mg. per 100 cc., being below 100 mg. most of the time. The spinal fluid sugar ranged between 14-45 mg. per 100 cc., and the cell count declined gradually to values between 6 and 20. No tubercle bacilli were obtained during this period. Of interest was the observation that administration of intrathecal streptomycin was associated with a profound rise of the total blood eosinophile count. These values fell to normal with cessation of this therapy.

At the age of 8 months the Mantoux test was first found to be faintly positive at 1:100. Radiographs taken during this period showed a severe exacerbation of his disease, with the reappearance of the diffuse miliary picture and some enlargement of the hilar nodes (Fig 8). In contrast with the original films the individual lesions were larger and "softer." Paraaminosalicylic acid was discontinued at this point and isoniazid substituted in a dose of 5 mg/kg/day. The pulmonary lesions cleared quite rapidly, and about two months after the tuberculin test had become positive the major x-ray finding was a profound emphysema which had been developing insidiously (Fig. 9). Through this entire period he had precariously maintained a weight of about 7 lb. Frequent transfusions of whole blood were required to maintain adequate hemoglobin levels, and excellent nursing care maintained his nutritional requirements. Supplementary nutriments were used lavishly. Accurate evaluation of his total development was difficult, but there was complete cessation of growth after the onset of symptoms, at 2 months of age, although in many ways he seemed alert and displayed some ability to learn. However, at the age of 10½ months a high spiking fever suddenly developed, and the infant lapsed into coma. The spinal fluid contained 900 lymphocytes, a highly elevated protein, and reduced sugar. Tubercle bacilli were subsequently obtained on culture. Intrathecal streptomycin was given only a few days, since it was soon apparent that death was inevitable. Convulsive movements became severe, and he died at 11 months of age.

At autopsy the body was extremely cachectic and measured only 55.5 cm. in length. The right pupil was dilated. Large submandibular nodes were present, but there was no other adenopathy. There was a marked increase in the anteroposterior diameter of the chest, with flaring of the inferior borders. The lungs were uniformly voluminous and emphysematous. No nodularity was present, and only a small amount of fibrosis in the right upper lobe gave evidence of a preexisting inflammatory process. The hilar and mediastinal nodes were not enlarged, and the thymus was atrophic. Neither the liver nor the spleen was beyond normal limits of size but both showed numerous small tubercles over the surfaces. The brain weighed 582 gm. Structures at the base of the brain were completely obscured by a thick tenacious exudate that extended laterally and encroached upon the lateral and inferior portions of the hemispheres. The right hemisphere was slightly larger and softer than the left. The right ventricle was found to be dilated and the ependymal surfaces studded with

Fig. 9.—Case 5, x-ray Dec. 3, 1952, taken shortly before death. Little sign of tuberculous disease remains except severe emphysema.

tiny miliary tubercles. The left ventricular system was completely occluded by a thick gelatinous exudate that extended into the third ventricle. The right intraventricular foramen was occluded, apparently by pressure from the large amount of exudate in the left ventricle. The aqueduct was patent, but the same gelatinous material filled the fourth ventricle. The posterior portion of the left hemisphere was softened, and a large subependymal mass of gelatinous material was found to be continuous with the material filling the ventricles.

Microscopically it was impossible in most areas of the lung to recognize any specific lesions characteristic of tuberculosis, although a few fibrotic, well-healed miliary tubercles, occasionally showing giant cells, were seen. Acid-fast organisms could not be found. The most characteristic and frequent changes were small linear areas of fibrosis seen in proximity to septa, blood vessels, and small bronchi

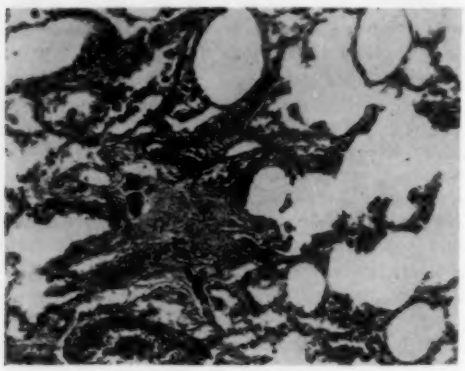


Fig. 10.—Case 5, photomicrograph of lung showing typical area of fibrosis.

(Fig. 10). Most of these were acellular and avascular. In some, however, residual islands of atelectatic alveoli with cuboidal epithelial cells and mild lymphocytic infiltrations could be found. The degree of emphysema seen microscopically was proportional to the extent and frequency of these lesions. No evidence of caseation or calcification was found. The hilar nodes were partially fibrotic with only a few, well-healed tubercles being seen. The bronchi, blood vessels, and pleura were not involved. Relatively few healed tubercles were present in the spleen and liver. These were variably fibrotic, showing fibrinoid changes centrally and slight lymphocytic infiltrations peripherally. They were not vascularized, and no giant cells were found. Extensive hemosiderosis was present in both liver and spleen. Several multinucleated polygonal cells were found in the liver. No caseation or calcification was present, and acid-fast organisms could not be demonstrated in any organ except the brain. The remaining viscera contained no definite evidence of tuberculosis.

Sections through the left occipital focus showed it to be a large area of degenerating glial and neural elements and large numbers of polymorphonuclear leucocytes. The adjacent ependyma was eroded, and the neighboring surviving brain tissue was infiltrated with mononuclear cells and a few polymorphonuclear cells. The ependymal surfaces were found to be severely involved by typical miliary lesions, and large areas were eroded. The exudate filling the ventricles was a mucinoid material also containing numbers of inflammatory cells and necrotic glial and neuronal elements.

Comment.—This last case is in sharp contrast to Cases 1 and 2 in that a remarkable tenacity and response to infection was displayed, although all three children were comparable in respect to birth weight, mode of infection, and treatment. Of particular interest were the clinical manifestations of the immunologic response. There appears, first of all, to have been a high degree of "constitutional resistance," since the disease was not far advanced when first discovered, at 2 months of age, and the infant subsequently overcame the pulmonary infection. Secondly, he displayed almost complete healing of a typical miliary infection before the development of skin sensitivity, which, interestingly, did not become apparent until he was 8 months of age. At this time he developed pulmonary lesions which were thought to be pulmonary "tuberculin reactions" at the site of his healing miliary lesions. Finally, after surviving what would seem to be the more hazardous anergic phase of his existence, he developed a full-blown meningitis and died after 11 months of infection, leaving very little trace of the original disease, except in the central nervous system.

COMMENT

The term "congenital tuberculosis" has been avoided in this group of cases, since all appear to have acquired their infection by way of the respiratory tract either during birth or shortly thereafter. None of the cases satisfied Hughesdon's [1] criteria for congenital infection. Case 1 was novel in that exposure to infection must have been quite brief, since only one of the twins was infected. The

course of the disease in this case was extremely rapid and overwhelming, and it is remarkable that the sibling was not also infected. The fourth infant was born at term and probably acquired his infection from his father. Cases 2, 3, and 5 were infants born prematurely of mothers that were undoubtedly ill at the time of delivery, and infection presumably occurred by aspiration during passage through the birth canal or during the short period of contact with the mother immediately following birth. The influence of maternal infection in producing premature labor is largely a matter for speculation. In none of the cases was the source of the infection discovered before the child was already seriously affected.

All of the cases showed evidence of extremely severe and widespread disease, characteristic of neonatal tuberculous infection. Undoubtedly, prematurity was, in itself, an important contributing factor to the fatal outcome of these cases, but it is interesting to note the wide range of response to the infection from case to case. Case 1 was most interesting and unusual and represents the extreme in its rapid evolution and lack of response. Here the lesions were anatomically distributed in a pattern typical of hematogenous infection, while the distribution of the intrathoracic lesions was typical of a primary tuberculous infection. Microscopically, these were multiple areas of necrosis, with a relatively scant mononuclear-cell reaction. Nowhere was any evidence of giant-cell or tubercle formation seen, although the lesions were teeming with acid-fast organisms. The severe degree of liver damage was unusual, even in view of the character of the infection, and indicates the fulminating nature of this patient's infection. Cases 2, 3, 4, and 5 had lesions characteristic of far-advanced, active, progressive disease. All, however, showed some evidence of healing, not related to "organ resistance," but more probably related to the administration of specific antibiotics. The complete absence of active pulmonary disease at the time of death in Case 5 was remarkable. That most of the lesions had healed with the aid of specific therapy prior to the development of skin sensitivity points to the multiplicity of factors responsible for "immunity" in tuberculous infection. All of the cases showed an extensive emphysema in the less-involved portions of the lung, and this may be expected to be of major concern in those children who survive.

The major interest in this group lies in the age and, more particularly, the birth weight of the patients. In general the premature infants showed the same response to infection as the term infant in this group and those seen elsewhere in that the disease was overwhelming, progressive, and fatal. While it is likely that physiologic immaturity contributed considerably to the fatal outcome of our series, certain clinical features are of interest.

All five cases developed significant symptoms at 6-8 weeks of age and, in most, acute symptoms followed a relatively asymptomatic period of what seemed to be normal growth and development. Only in retrospect were tendencies to thermal lability, occasional low-grade temperature elevations, intermittent periods of lethargy, and mild respiratory tract infections noted prior to the onset of acute symptoms. Thick nasal discharge, nonproductive cough, lethargy, low-grade fever, and some anorexia were among the commonest findings marking the onset of clinically obvious disease. Following this, in our treated groups, the weight curve generally flattened but was maintained at approximately uniform levels until the days approaching death. Severe anemia was frequent, and repeated transfusions of whole blood were required to maintain adequate hemoglobin levels. It will be noted that transient elevations in spinal-fluid protein were common in these cases, although pleocytosis and decreased spinal fluid sugars were not present in Cases 2, 3, and 4.

Tuberculin sensitivities in this group in general appear to be related to birth weight. While the term infant showed a positive skin test at the onset of symptoms, this is not a consistent finding in a larger experience with term infants acquiring tuberculous

infection. Case 3 required a dilution of OT. 1:500 to demonstrate sensitivity, and Case 2 never showed skin sensitivity, although concentrations greater than 1:1000 were not used. Case 5 deserves special consideration because a positive skin test did not develop until 8 months of age and after almost complete resolution of the pulmonary lesions had occurred.

Case 5 was of special interest because of several rather unusual features to be observed. Probably of fundamental significance was the development of tuberculin sensitivity in this patient. When disease was first suspected the child already had a typical miliary tuberculosis with an area of consolidation. Even after treatment was begun there was some extension of his pulmonary disease before he slowly began to show some improvement. By 7 months of age there was practically no trace of tuberculous disease by x-ray. Yet the OT. remained negative until 8 months of age, when he developed definite skin sensitivity and there was an acute flare-up of the miliary lesions. These, however, cleared quite rapidly, indicating that they were essentially tuberculin reactions around old lesions, secondary to the development of sensitivity rather than a recurrence of miliary lesions. This transient flare-up was probably not due to the administration of tuberculin, since the infant had been showing increased systemic symptoms for about two weeks prior to the test and the films showing the pulmonary flare-up were taken on the day before the first positive skin test. The development of meningitis may have been brought on by the break-down of an intracranial lesion following development of sensitivity. This event was not halted by the use of isoniazid, which was then first available at the time skin sensitivity appeared.

A variety of therapeutic programs were followed, since these cases were seen through the recent period of development of the various antituberculous agents. No attempt at determination of efficacy can be made with a series of this type, except to note that therapy was obviously inadequate. In this regard, two factors should be considered. In none of the cases was treatment started until significant pulmonary lesions, and usually symptoms, had developed, chiefly because symptoms were minor and noted only because of illness in the parent. It is also possible that, with the agents used, the usual dosages are inadequate under the conditions present in this group. Hence it seems that improvements in results will come from early institution of therapy in suspected cases, as was done with the first of Kendig's three cases.* This will require not only adequate maternal supervision but a discriminating suspicion with close attention to subtle changes in the progress of the child. One probably cannot hope to fulfill many of the usually desired diagnostic criteria, such as a positive Mantoux, characteristic radiographic changes, and a demonstrable organism, before starting therapy if the interim between infection and therapy is to be reduced. In this group the major diagnostic criteria present before the onset of acute symptoms were (1) tuberculous disease in the mother or family, (2) compatible but not necessarily diagnostic roentgen changes, and (3) subtle variations in temperature, appetite, and activity.

When the presence of active tuberculous infection is known to exist in the mother, vigorous therapy of the newborn infant should be started immediately. If there is a known contact, the slightest aberration in the clinical course should arouse a strong suspicion of possible infection of the infant.

SUMMARY

Five fatal cases of tuberculosis occurring in the neonatal period are presented and correlated with the autopsy findings. Four of the patients were premature infants. While all of the infants eventually died, a wide range of response to the infection was seen in the clinical and pathological studies, indicating that a more favorable outcome should be expected in such a group, providing an increased diagnostic and therapeutic vigor commensurate with the seriousness of the

* References 2 and 3.

condition can be maintained. It is apparent that an improved prognosis will require an awareness of the entire problem of infection in the neonatal period, continuous effort to discover the presence of tuberculous infection in mothers and contacts, and prompt, vigorous therapy based on reasonable suspicion rather than on an absolute diagnosis of active tuberculous disease.

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Use of Reference Tables in Fluid Therapy of Diarrheal Dehydration

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The great advances made in our understanding of the disturbances in fluid balance in many diseases have had the unfortunate consequence of making the subject increasingly complex for the practicing physician. Application of available knowledge requires a discouraging amount of calculation, which becomes easy only through constant use. It would thus seem desirable to have some simplified therapeutic scheme which obviates the need of much calculation but which continues to emphasize the basic therapeutic principles concerned with repair of deficits and with prevention of further deficits through the addition of fluids appropriate for maintenance.

We have for a number of years employed an outline of fluid therapy for the guidance of resident staff and students. Originally patterned in large part on the recommendations of Butler and Talbot,* it has been periodically revised and amplified and has proved very useful in training the staff in the management of a variety of disturbances affecting fluid equilibrium. The plan, however, remained open to the objection that it necessitated much calculation and thorough familiarity with many details.

Recently we have added one feature to the outline which overcomes the objection mentioned. It consists of a series of reference tables for the intravenous treatment of diarrheal dehydration, specifying the exact amounts and kinds of solutions to be used as well as the order of their administration and the rate of flow to be employed. It encompasses a weight range in infancy and childhood from 2 to 20 kg. and requires that the physician obtain only the value of the CO_2 combining power of the blood and that he make a clinical appraisal of the severity of the dehydration present. Provision is made for the short-term management of easily controlled cases as well as for the prolonged and continuous treatment of protracted or relapsing types of diarrheal disease.

We are presenting the tables together with a discussion of the theoretical basis for the recommendations which are made. In addition we have appended a description of some of the technical details involved in the successful administration of fluids by means of a continuous intravenous drip. The plan is based upon the assumption that one can in each case make a clinically satisfactory estimate of the water and electrolyte losses and that optimal treatment should aim at the more or less complete correction of some deficits within the first 24 hours, at the partial correction of others, and at halting or minimizing the unfavorable balance of the remaining electrolytes. Oral intake of food and fluids is completely withheld for a minimum of 24 hours. When feedings are reinstituted the method of step-wise increase originally propounded by Finkelstein [3] and emphasized in this country by Powers [4] is followed. During the period of suboptimal feeding the fluids necessary for maintenance are supplied intravenously.

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* References 1 and 2.

In addition to blood or plasma varying amounts of four solutions, namely, isotonic saline, dextrose in water, M/6 sodium lactate, and 15% potassium chloride, are employed. During the first 24 hours the order of administration of suitable mixtures of the fluids is dictated by the priority of certain physiologic goals as well as by the necessity of waiting for the typing and cross matching of blood and for the determination of the blood CO_2 combining power. Thereafter the fluid requirement for 24-hour periods is readily determined and can be met by administration of a single mixture of desired electrolytes.

Intelligent use of the tables presupposes some familiarity with the nature of the losses resulting from diarrhea and the manner of estimation of the quantities of water and electrolytes needed for repair of the deficits and for maintenance of the patient during periods of starvation and of suboptimal feeding. For this reason we shall first describe in some detail the theoretical considerations involved and how they are applied in the specific treatment of a hypothetical case. The appropriate calculations will be discussed at the same time.

DEFICITS RESULTING FROM DIARRHEA

Water Loss.—Estimation of the water loss occasioned by diarrhea affords a basis for the calculation of the reparative goal of the first 24 hours. It is assumed that acute weight loss is a measure of fluid loss. Where the weight of the patient before onset is not accurately known, the loss is estimated in the following manner. Since clinical evidence of dehydration becomes readily detectable when there has been a loss of 10% of body weight, this figure is taken to represent the minimal loss in any patient with diarrhea of a magnitude warranting intravenous therapy. Severe diarrhea may result in loss of 15% of body weight. We have adopted these two figures, 10% and 15%, to represent the range of water loss in diarrhea and have added the intermediate one of 12.5% in order to establish three categories of cases of varying severity.

Sodium Deficit (Extracellular Water Loss).—Metabolic observations in fasting,[5] thirsting,[6] diarrhea,† and diabetic acidosis,‡ all point to a sharing of losses of water from the body more or less equally by the intracellular and extracellular compartments. Therefore,

$$\frac{\text{Estimated weight loss (gm.)}}{2} = \text{ml. extracellular sodium-containing fluid lost (ECW)}$$

The figure thus obtained is considered to measure the total deficit of extracellular water (ECW) in need of replacement in the first 24 hours. The crude substitute for ECW to be used for this purpose consists of a mixture of one part of M/6 sodium lactate solution and five parts of isotonic saline. The concentrations of the component ions in the mixture are sodium 149 mEq., chloride 121 mEq., and lactate 28 mEq. per liter.

Bicarbonate Deficit. — In addition to shrinkage in size of the extracellular fluid compartment of the body diarrhea is responsible for disproportionately large losses of bicarbonate with resulting acidosis. For correction of the deficit we have not employed the standard formula § (or one of its derivative expressions), since it is likely to give an excessively high figure for lactate. It is believed that incomplete correction of acidosis is less to be feared than overcorrection, which, by producing alkalosis, may entail the danger of a low-potassium syndrome or of tetany. For this reason the formula is modified to take account only of

† References 7 and 8.

‡ References 9 and 10.

§ According to this formula, milliliters of M/6 lactate per kilogram required for correction of acidosis = $(25\text{-}CO_2\ [\text{in milliequivalents}]) \times 0.7 \times 6$, in which 25 represents the normal concentration of bicarbonate in milliequivalents per liter, 0.7 the liters of water per kilogram of body weight, and 6 the factor for correction of the diluted lactate solution. Calculations based on the formula involve the assumption that the bicarbonate level in intra- and extracellular fluids is the same, which is incorrect, and that the rise in bicarbonate level after lactate administration occurs with equal facility in both extra- and intracellular compartments, which is challenged (References 11 and 12).

the bicarbonate deficit of the shrunken extracellular compartment (here assumed to be reduced to 20% of the body weight). The changed formula with a correction goal for bicarbonate of 20 mEq. per liter becomes (20-CO_2 [in milliequivalents]) × 0.20 × 6 = ml. M/6 lactate per kilograms.‖

Potassium Deficit. — Balance studies of Darrow and co-workers [8] have shown that potassium deficits in acute diarrhea are of the same order of magnitude (approximately 10 mEq. per kilogram of body weight) as the sodium losses. A part (perhaps one-half) of the potassium loss accompanies breakdown of protein and need not be considered for immediate replacement. Complete replacement of the remainder apparently cannot be achieved within 24 hours and in any event would entail the use of dangerously large amounts of potassium. The recommended dose for repair is 2.8 mEq. per kilogram of body weight. The figure was originally obtained by Darrow [13] by calculating as a safe dosage that amount of potassium chloride which, if not preferentially absorbed by the cells, would raise the level of potassium in the body fluids by not more than 4 mEq. per liter. Potassium would thus fail to attain a lethal concentration in the plasma. The calculation was as follows: 4 mEq/liter (i. e., the permissible increment of potassium in body water) × 0.7 liters (representing the total water per kilogram body weight) = 2.8 mEq. per kilogram. In actual practice this amount of potassium has proved safe and effective for the limited objective of prevention of hypopotassemia and reduction of undesirable intra- and extracellular shifts of cations.

CALCULATION OF MAINTENANCE REQUIREMENTS

The amounts of water and electrolytes supplied in the first 24 hours of treatment for the repair of earlier deficits must be augmented in order to meet the normal maintenance requirements for this period. If continuation of parenteral fluid therapy on subsequent days proves necessary the fluid needs of the patient are usually adequately met by satisfying the maintenance requirements alone. It has been found that these requirements show a close correlation with the surface area of the body. The following figures representing basal needs are from the metabolic studies of Butler [10] and Gamble.[6]

Water—850 ml/square meter

Sodium—10 mEq/square meter (70 ml. isotonic saline/square meter)

Potassium—12 mEq/square meter (0.90 gm. KCl/square meter)

These figures are calculated for minimal heat production, minimal sweating, minimal renal load (i. e., with the subject receiving oral water and dextrose), and maximal urinary concentration. For larger caloric output, moderate sweating, and minimal urinary concentration (slightly above that of glomerular filtrate) the water and electrolyte requirements are substantially larger. The water requirement estimated by the method of Darrow and Pratt [14] for nonprotein parenteral feeding, urine specific gravity 1.012, and caloric expenditure of 1500, is divided as 630 ml. insensible water loss, 850 ml. renal excretion, and 320 ml. loss in sweat. The larger figures which we have adopted for sodium and potassium represent arbitrary increases to serve on the one hand as a safety factor against unusual losses through sweating and the occasional persistence of loose stools beyond the first 24 hours and on the other hand to provide for the increased urinary excretion of potassium in response to stress. Thus modified the figures become as follows:

Water—1800 ml/square meter

Sodium—29 mEq/square meter (200 cc. isotonic saline/square meter)

Potassium—23 mEq/square meter (1.7 gm. KCl or 11.5 ml. 15% KCl solution/square meter)

‖ It will be seen that lactate is here employed to supply the deficit of bicarbonate ions in the existing extracellular compartment, whereas the lactate discussed in the preceding section is one of the ions administered for the purpose of reexpansion of the extracellular compartment.

PARENTERAL TREATMENT OF DIARRHEA
(FIRST TWENTY-FOUR HOURS)

An illustrative example of fluid therapy including the order of administration of the solutions used may be considered at this point. The hypothetical case is that of an infant weighing 5 kg. (surface area = 0.27 sq. m.) on admission and estimated to have suffered an acute loss of 12.5% of body weight due to diarrhea. Since this is merely a guess it is unnecessary to compute his weight before illness (in this example 5.7 kg.). Instead all calculations are based on the admission weight. Thus:

[1] 5 kg. × 0.125 = 0.625 kg. weight loss = 625 ml. fluid loss.

[2] 625/2 = 313 ml. isotonic sodium-containing fluid to be replaced.

For this purpose ⅙, equal to 52 ml., M/6 lactate solution and ⅚, equal to 261 ml., isotonic saline will be used.

[3] 0.27 sq. m. × 200 ml. (maintenance sodium) = 54 ml. isotonic saline, added to meet the daily requirement.

[4] Total [2] + [3] = 367 ml. isotonic sodium-containing fluid to be given, of which 261 (from [2] + 54 (from [3], or 315 ml., is to be given as isotonic saline.

[5] Total water loss (from [1]) = 625 ml. This figure is employed even though correction of water balance demands complete correction of intra- and extracellular electrolyte structure. As a matter of fact the water correction for the intracellular compartment which can theoretically be achieved by the dosage of potassium employed is something less than one-third the loss. In this example approximately 200 ml. of the 625 ml. water deficit will be supplied without electrolyte to hold it within the cells. It is probable that this portion of the water can be dispensed with, but its inclusion in the therapeutic plan here serves a twofold purpose. It may prove beneficial for cases exhibiting hyperosmolarity of the plasma as a result of hyperventilation, sweating, or excessive loss of hypotonic intestinal secretions and may act as a safeguard against the dehydrating effect of occasional large losses of water through continued sweating.

[6] Maintenance water (1800 ml. per square meter × 0.27 square meter) = 486 ml.

[7] Total water requirement ([5]+[6])= 1111 ml., to be given in part as electrolyte solution with the remainder as 5% dextrose in water.

[8] Potassium requirement 2.8 mEq. × 5 kg. = 14 mEq. Here one departs from the principle of adding the maintenance requirement to the amount designated for repair, since such a combined total is undesirably large. The solution of potassium chloride employed (15% concentration) contains approximately 2 mEq. per milliliter. Therefore 7 ml. is the required amount.

[9] Blood or plasma (300-400 ml/square meter × 0.27 sq. m. = 81-108 ml.). One of these may be added to the therapeutic regimen for the first 24 hours in the severer cases manifesting shock. The water and electrolyte content of these fluids are omitted from the calculations. However, in those patients receiving repeated transfusions of plasma on subsequent days it becomes essential to take account of the electrolyte content.

[10] Total fluids excluding blood or plasma and a corrective addition of sodium lactate [7], 1111 ml.

[11] Total isotonic sodium-containing fluids not including the as yet undetermined amount of sodium lactate to be added for correction of bicarbonate deficit [4], 367 ml.

[12] Total potassium and dextrose solutions, by difference, 744 ml.

All of the foregoing calculations in our hypothetical case are made on admission of the patient. After withdrawal of blood for determination of the CO_2 combining power and for typing and cross matching the initial step in treatment is taken. This consists in the administration over a period of three hours of a mixture containing one part M/6 sodium lactate solution, two parts isotonic saline, and three parts 5% dextrose in water. In conformity with recommendations made by Butler [10] for preliminary hydration of cases of diabetic acidosis we have adopted the figure of 1050 ml. per square meter as the volume of fluid to be administered. The rate of infusion for the first 90 minutes is 8 ml. per minute per square meter. The primary objectives here are rapid restoration of blood volume and initiation of diuresis. The high content of lactate in the solution serves also to effect early amelioration of the acidosis. In the present example the amount of the mixture (1050 ml. × 0.27 sq. m.) is 284 ml. and the initial rate (8 ml. × 0.27 sq. m.) is 2.2 ml., or about 30-35

drops per minute. At the end of 90 minutes, approximately two-thirds of the total, corresponding to the dosage of 700 ml. per square meter recommended by Butler, will have been given. The infusion of the remainder of the mixture is continued at a reduced rate of flow, approximately 3-4 ml. per minute per square meter. The calculation in the present example is 4 ml. × 0.27 sq. m. = 1.1 ml., or about 15-17 drops per minute. Since the remaining volume of fluid and the rate of flow are both reduced to one-half that of the initial period, it will be seen that the time consumed in administration will likewise be about 90 minutes.

By this time the preparations for the transfusion of those patients requiring treatment for shock will have been completed. The bottle and tubing may now be rinsed with a small volume of saline solution to remove the dextrose. This procedure is followed by administration of the appropriate amount of blood. In the present example the dosage range was found to be 81-108 ml., and 100 ml. is given. The rate of flow is unchanged at 3-4 ml. per square meter per minute.

The report of the CO_2 combining power supplies the data requisite for the final calculations. It is assumed in the illustrative case that the concentration of CO_2 was found to be 5 mEq. per liter. Then (20—5) × 0.20×6 = 18 ml. M/6 lactate per kilogram represents the amount which must be administered to correct the bicarbonate deficit. This figure multiplied by the weight of the infant (5 kg.) gives the required amount as 90 ml. This amount added to the 52 ml. (from [2]) supplied for rehydration of the extracellular compartment gives a total lactate requirement of 142 ml. The patient has, however, already received 47 ml. in the initial fluid mixture.¶ He has also received 94 ml. of isotonic saline and 142 ml. of dextrose in water.

There remain to be given the following:

Balance sodium lactate solution (142-47) = 95 ml.
Balance sodium as isotonic saline (315-94) = 221 ml.
(315 represents the total volume of isotonic saline for repair plus maintenance (from [4]) and 94 ml. the volume of saline already given)
Balance 5% dextrose in water (744-142) = 602 ml.
(744 ml. represents the total volume of dextrose in water to be administered and 142 ml. is the volume already given)
Total volume of remaining fluids to be given (95 + 221 + 602) = 918 ml.

These solutions are accordingly mixed in a large sterile flask and administered during the remainder of the 24 hours. The rate of flow is now further slowed so that the fluid will be continuously administered over the entire period (918 ml. divided by 19.5, or 21 hours, depending upon whether blood was or was not given). The rate becomes 11 to 12 drops per minute. As soon as adequate voiding occurs it is safe to add the calculated volume of potassium chloride solution, in this instance 7 ml., to the contents of the bottle. It will be assumed here that satisfactory diuresis was established after the patient received an additional 100 ml. of fluid. The potassium chloride when added to the remaining volume of 818 ml. gives a concentration of potassium of 17 mEq. per liter.

PARENTERAL TREATMENT OF DIARRHEA AFTER THE FIRST TWENTY-FOUR HOURS

Considerable divergence in the management of cases is possible after the first 24 hours. In older infants and children one may usually initiate a regimen of oral feedings of low caloric content combined with dilute electrolyte solutions. Intravenous therapy in such cases is no longer necessary. In very young infants, on the other hand, the institution after 24 hours of feedings with progressive daily increases in caloric content has frequently resulted in troublesome or dangerous relapses of the diarrhea. We have pre-

¶ The lactate solution initially given to an infant weighing 5 kg. is sufficient for the correction of a bicarbonate deficit of 4.7 mEq. per liter. Because of the discrepancy inherent in administering fluids on the basis of surface area and calculating bicarbonate deficits on the basis of weight the initial fluids provide for a variable correction of bicarbonate deficit ranging from 3.3 mEq. per liter in the larger children to 6.2 mEq. per liter in the smallest infants. This variable correction proves to be generally desirable, since the smallest infants are likely to have the severer bicarbonate deficits.

ferred therefore to continue intravenous administration of fluids in small infants for two to four days and at some time during this period, usually on the third day, to begin offering minimal amounts of milk in a most cautious manner.

In all cases the water and electrolyte requirements must be satisfied. Ordinarily minor modifications of the amounts obtained from the calculation of maintenance needs are sufficient for this purpose. Thus in the illustrative example of the infant weighing 5 kg.:

Water requirement (1800 ml. per square meter × 0.27 square meter) = 486 ml. If the infant is receiving nothing by mouth the figure of 486 ml. is unchanged. If small feedings are instituted the daily water intake may be increased to allow for the increased renal excretion incident to protein feeding. Again applying the principle of liberality to permit of minimal urinary concentration, recalculation of the renal water requirement under conditions of full dietary intake gives a figure of 1350 ml. per square meter as compared with 850 ml. per square meter for protein-free fluid administration. Thus the total daily water requirement is increased from 1800 ml. per square meter to 2300 ml. per square meter. In the illustrative case the higher water requirement (2300 ml. per square meter × 0.27 square meter) becomes 621 ml.

Sodium requirement (29 mEq. per square meter × 0.27 square meter) = 7.8 mEq. or, for isotonic saline, (200 ml. per square meter × 0.27 square meter) = 54 ml. Additional sodium as M/6 lactate solution in an amount determined after applying the formula, (25-CO_2 in mEq.) × 0.25 × 6, for correction of bicarbonate deficits may be administered if the CO_2 combining power is found to be below 18 mEq. per liter.

Potassium requirement (23 mEq. per square meter × 0.27 square meter) = 6.2 mEq. Because of the known deficit of potassium remaining after the first 24 hours of treatment the amount may be increased to 30 mEq. per square meter. Then 30 mEq. × 0.27 square meter = 8.1 mEq. or 4.1 ml. of 15% potassium chloride solution.

Assuming in the illustrative case that feedings are completely withheld during the second 24 hours of treatment one would administer a total of 486 ml. of fluid, consisting of 54 ml. isotonic saline, 428 ml. of 5% dextrose in water, and 4.1 ml. of 15% potassium chloride solution. Addition of appropriate amounts of water-soluble vitamins is optional. The concentration of potassium in the fluid mixture is 17 mEq. per liter. It may be noted further that the electrolyte content (sodium 8 mEq., potassium 8 mEq., and chloride 16 mEq.) is such that a considerable excess of chloride is present. Although there is little likelihood of difficulty on this score in the case of older infants or children it is well to check the bicarbonate content of the plasma at intervals. In newborn or premature infants all, or a portion, of the saline may be replaced by an equivalent amount of M/6 lactate solution, since the need for chloride is fully met by the potassium chloride alone.

In many cases it is possible to carry out oral feeding of small amounts of a milk formula diluted to a volume sufficient to meet the daily need for water. In such cases the necessary solution of electrolytes in the form of isotonic saline and potassium chloride solution may be used as a diluent for the milk. When the intake of food is increased to the point where the patient is receiving about 50% of the normal caloric requirement in the form of cow's milk, the addition of electrolyte solutions may be discontinued.

PROLONGED PARENTERAL FLUID ADMINISTRATION IN INFANTS

Occasionally it is necessary to maintain infants for more than a few days on a regimen of exclusive parenteral feeding. Since some of these infants may be in a poor nutritional state, it is desirable to prevent or minimize further breakdown of nitrogen. Unfortunately the simple addition of plasma protein or of amino acids to the fluid regimen is followed merely by their normal oxidation as added foodstuffs. The special role of protein in preservation of the protoplasmic structure of the body is thus bypassed, and endogenous nitrogen breakdown is not affected. In order to halt the negative nitrogen balance it appears to be necessary to give the patient from 60% to 70% of his caloric requirement in the form of carbohydrate

(or of carbohydrate and fat) in addition to his basal requirement of protein.[6] The manner in which 10% dextrose solutions and plasma may be employed to meet this objective may be seen in the following calculations.

Carbohydrate requirement as 10% dextrose solution 2625 ml. per square meter (1500 Cal. per square meter × 70% = 1050 Cal., which is the amount obtainable from 262.5 gm. dextrose or 2625 ml. 10% dextrose solution).

Protein requirement 25 gm. per square meter. This is intended to meet the basal need as contrasted with the amount for normal growth. In terms of plasma containing 7% protein the requirement would be 360 ml. per square meter.

Illustrative example, infant weighing 5 kg., surface area 0.27 square meter.

Carbohydrate as 10% dextrose solution (2625 ml. per square meter × 0.27 square meter) = 709 ml. It is apparent that when the carbohydrate requirement is supplied in the form of 10% dextrose solution the water needs (2300 ml. per square meter) are more than adequately met.

Protein as plasma (360 ml. per square meter × 0.27 square meter) = 97 ml.

Sodium (200 ml. isotonic saline per square meter × 0.27 square meter) = 54 ml. It will be noted that the sodium content of plasma including the content of sodium citrate added as anticoagulant is 17 mEq. per 100 ml. From this it is evident that the dosage of plasma employed supplies more than twice the calculated sodium requirement (8 mEq.). While this amount given daily to infants with normal renal function has been well tolerated, attempts on our part to give substantially larger volumes of plasma in order to increase the protein intake have resulted in the clinical appearance of edema.

Potassium (23 mEq. per square meter × 0.27 square meter) = 6.2 mEq. This amount is present in 3.1 ml. of 15% potassium chloride solution.

Water-soluble vitamins in appropriate amounts are added.

USE OF THE REFERENCE TABLES

Tables 1 to 6, inclusive, epitomize the information outlined in the preceding pages. It will be noted that Table 1 supplies data pertaining to the initial treatment of all cases. Tables 2 to 5 are concerned with the remainder of the therapy during the first 24 hours. The division of the data into four tables reflects the variation in fluid administration for the correction of different degrees of dehydration. Thus, in Tables 2 and 3 are found the recommendations applying to patients with dehydration estimated to have resulted in a 10% loss of body weight. Similarly Tables 4 and 5 incorporate the figures appropriate for the severer degrees of dehydration amounting to losses of 12.5% and 15% of body weight, respectively. Tables 2-5, inclusive, are further subdivided to provide for the correction of CO_2 values ranging from 5 to 15 mEq. per liter. Finally, in Table 6 are listed the amounts of the different solutions used for daily maintenance under both short-term and long-term plans for parenteral therapy.

Inspection of the Tables discloses columns for both weight and surface area, the latter determined for infants and children of normal body proportions from the nomogram of Hannon.[15] For practical purposes it is sufficient to employ the figures in the weight column to determine the fluids appropriate for the patient with average body contour. In certain instances of unusual body proportions the determination of the patient's body surface area may assume importance. It is well to point out, therefore, that Tables 1 and 6 are based entirely on surface area measurements, while Tables 2-5, by virtue of the calculations for fluid loss and bicarbonate deficits, are largely based on the weight of the patient.

The initial step in treatment consists in the intravenous administration of the mixtures of isotonic saline, M/6 lactate solution, and dextrose in water specified in Table 1 for the weight category nearest to that of the patient. The fluid is infused for the first 90 minutes at the rapid rate indicated in the sixth column of the Table. Thereafter the rate is slowed in accordance with the figure in the seventh column. If the patient is deemed to be in shock, blood is administered in accordance with the specifications found in the last column of the Table. It may be observed that the volumes of the various solutions are expressed in round numbers, namely, to the nearest 5 or 10 ml. figure.

TABLE 1.—*Therapy for Diarrheal Dehydration, First Three Hours*

Weight, Kg.	Av. Surface Area, Sq. M.	Fluid Mixture No. 1					Fluid No. 2, Blood, Ml.†
		Isotonic Saline, Ml.	M/6 Lactate, Ml.	5% Dextrose, Ml.	Initial Rate, Drops/ Min.*	Rate After 1½ Hr., Drops/ Min.	
2.0	0.14	50	25	75	16	8	50
2.5	0.16	55	30	85	19	9	55
3.0	0.19	65	35	100	22	11	65
3.5	0.21	75	35	110	24	12	75
4.0	0.23	80	40	120	26	13	80
4.5	0.25	85	45	130	29	14	85
5.0	0.27	95	45	140	31	15	95
5.5	0.29	100	50	155	34	17	100
6.0	0.31	110	55	165	36	18	110
7.0	0.35	120	60	185	40	20	120
8.0	0.38	135	65	200	44	22	135
9.0	0.42	150	75	220	50	25	150
10	0.46	160	80	240	54	27	160
12	0.52	180	90	270	60	30	180
14	0.58	200	100	300	66	33	200
16	0.65	230	115	340	76	38	230
18	0.70	240	120	370	83	41	240
20	0.77	270	135	400	90	45	270

* Rates in ml./hr. are readily calculated by multiplying drops/min. by the factor 4.

† Use of blood is optional and depends on the presence of obvious or suspected shock. Rate of administration is the same as the slow rate for fluid mixture No. 1, indicated in the column immediately to the left.

The composition of the fluid mixture employed during the remainder of the first 24 hours is found by referring to those parts of Tables 2-5 appropriate for the estimated degree of dehydration and for the value of CO_2. Since exact correction of the acidosis is not possible with the aid of crude mathematical calculations and since such correction is distinctly secondary in importance to the need for rehydration, the Tables present only a few representative values for CO_2. It becomes necessary, therefore, to select the value for CO_2 which most nearly approaches that determined by analysis of

TABLE 2.—*Therapy for Diarrheal Dehydration, Remainder of First Twenty-Four Hours—Estimated Dehydration Equal to 10% of Body Weight*

Weight, Kg.	Fluid Mixture No. 3								
	CO_2, 7.5 mEq.					CO_2, 10 mEq.			
	Isotonic Saline, Ml.	M/6 Lactate, Ml.	5% Dextrose, Ml.	15% KCl, Ml.*	Rate, Drops/ Min.†	Isotonic Saline, Ml.	M/6 Lactate, Ml.	5% Dextrose, Ml.	15% KCl, Ml.*
2.0	60	20	250	3	4	60	15	250	3
2.5	80	30	295	4	5	80	20	295	4
3.0	100	35	355	4	6	100	25	355	4
3.5	115	45	400	5	7	115	35	400	5
4.0	135	55	450	6	8	135	40	450	6
4.5	150	60	495	6	9	150	45	495	6
5.0	165	70	540	7	9	165	55	540	7
5.5	185	80	585	8	10	185	60	585	8
6.0	200	85	630	8	11	200	65	630	8
7.0	240	105	725	10	13	240	80	725	10
8.0	275	120	810	11	15	275	100	810	11
9.0	310	135	900	13	17	310	110	900	13
10	350	155	995	14	19	350	125	995	14
12	420	190	1,160	17	22	420	155	1,160	17
14	500	225	1,330	20	25	500	185	1,330	20
16	570	260	1,500	22	29	570	210	1,500	22
18	650	300	1,650	25	32	650	245	1,650	25
20	720	330	1,830	28	35	720	270	1,830	28

* Dosage of potassium in milliequivalents equals ml. KCl multiplied by 2.

† Figures for rate of administration are approximate and apply to both the dosage scales for correction of CO_2 of 7.5 mEq. and of 10 mEq. Rates in ml./hr. are readily calculated by multiplying drops/min. by the factor 4.

TABLE 3.—*Therapy for Diarrheal Dehydration, Remainder of First Twenty-Four Hours—Estimated Dehydration Equal to 10% of Body Weight*

	Fluid Mixture No. 3								
	CO_2, 12.5 mEq.					CO_2, 15 mEq.			
Weight, Kg.	Isotonic Saline, Ml.	M/6 Lactate, Ml.	5% Dextrose, Ml.	15% KCl, Ml.*	Rate, Drops/ Min.†	Isotonic Saline, Ml.	M/6 Lactate Ml.	5% Dextrose, Ml.	15% KCl, Ml.*
2.0	60	10	250	3	4	60	5	250	3
2.5	80	15	295	4	5	80	5	295	4
3.0	100	15	355	4	6	100	10	355	4
3.5	115	25	400	5	7	115	15	400	5
4.0	135	30	450	6	8	135	15	450	6
4.5	150	35	495	6	8	150	20	495	6
5.0	165	40	540	7	9	165	25	540	7
5.5	185	45	585	8	10	185	30	585	8
6.0	200	50	630	8	11	200	30	630	8
7.0	240	60	725	10	12	240	40	725	10
8.0	275	75	810	11	14	275	50	810	11
9.0	310	80	900	13	16	310	55	900	12
10	350	95	995	14	18	350	65	995	14
12	420	120	1,160	17	21	420	80	1,160	17
14	500	145	1,330	20	24	500	100	1,330	20
16	570	160	1,500	22	27	570	115	1,500	22
18	650	190	1,650	25	31	650	140	1,650	25
20	720	210	1,830	28	35	720	150	1,830	28

* Dosage of potassium in milliequivalents equals ml. KCl multiplied by 2.

† Figures for rate of administration are approximate and apply to both the dosage scales for correction of CO_2 of 12.5 mEq. and of 15 mEq. Rates in ml./hr. are readily calculated by multiplying drops/min. by the factor 4.

the patient's blood. Tables 2-5 include figures calculated to the nearest milliliter for KCl solution, which is incorporated in the whole fluid mixture after active renal excretion is reestablished. It need hardly be emphasized that the use of potassium salts in intravenous solutions gives added importance to the necessity of maintaining the rate of infusion within strictly defined limits. One should also mention the desirability of guard-

TABLE 4.—*Therapy for Diarrheal Dehydration, Remainder of First Twenty-Four Hours—Estimated Dehydration Equal to 12.5% of Body Weight*

	Fluid Mixture No. 3												
	CO_2, 5 mEq.					CO_2, 7.5 mEq.				CO_2, 10 mEq.			
Weight, Kg.	Isotonic Saline, Ml.	M/6 Lactate, Ml.	5% Dextrose, Ml.	15% KCl, Ml.*	Rate, Drops/ Min.†	Isotonic Saline, Ml.	M/6 Lactate, Ml.	5% Dextrose, Ml.	15% KCl, Ml.*	Isotonic Saline, Ml.	M/6 Lactate, Ml.	5% Dextrose, Ml.	15% KCl, Ml.*
2.0	80	30	275	3	5	80	25	275	3	80	20	275	3
2.5	105	40	325	4	6	105	35	325	4	105	25	325	4
3.0	130	50	390	4	7	130	40	390	4	130	30	390	4
3.5	150	65	445	5	8	150	55	445	5	150	45	445	5
4.0	175	75	500	6	9	175	60	500	6	175	50	500	6
4.5	200	85	550	6	10	200	70	550	6	200	55	550	6
5.0	220	95	605	7	11	220	80	605	7	220	65	605	7
5.5	245	105	655	8	12	245	90	655	8	245	75	655	8
6.0	265	115	705	8	13	265	100	705	8	265	80	705	8
7.0	315	140	815	10	16	315	120	815	10	315	95	815	10
8.0	360	160	910	11	18	360	140	910	11	360	115	910	11
9.0	405	180	1,015	13	20	405	155	1,015	13	405	125	1,015	13
10	455	205	1,120	14	22	455	175	1,120	14	455	145	1,120	14
12	550	250	1,310	17	26	550	215	1,310	17	550	180	1,310	17
14	645	300	1,500	20	30	645	256	1,500	20	645	215	1,500	20
16	735	340	1,700	22	34	735	290	1,700	22	735	245	1,700	22
18	835	390	1,875	25	38	835	340	1,875	25	835	285	1,875	25
20	925	435	2,080	28	43	925	375	2,080	28	925	315	2,080	28

* Dosage of potassium in milliequivalents equals ml. KCl multiplied by 2.

† Figures for rate of administration are approximate and apply to the dosage scales for correction of each of the 3 degrees of acidosis in the table. Rates in ml./hr. are readily calculated by multiplying drops/min. by the factor 4.

TABLE 5.—*Therapy for Diarrheal Dehydration, Remainder of First Twenty-Four Hours—Estimated Dehydration Equal to 15% of Body Weight*

	Fluid Mixture No. 3								
	CO_2, 5 mEq.					CO_2, 7.5 mEq.			
Weight, Kg.	Isotonic Saline, Ml.	M/6 Lactate, Ml.	5% Dextrose, Ml.	15% KCl, Ml.*	Rate, Drops/ Min.†	Isotonic Saline, Ml.	M/6 Lactate, Ml.	5% Dextrose, Ml.	15% KCl, Ml.*
2.0	105	35	300	3	5	105	30	300	3
2.5	135	45	360	4	7	135	40	360	4
3.0	160	55	430	4	8	160	50	430	4
3.5	185	70	490	5	9	185	60	490	5
4.0	215	80	550	6	10	215	70	550	6
4.5	245	90	610	6	11	245	80	610	6
5.0	270	110	665	7	13	270	95	665	7
5.5	300	120	720	8	14	300	100	720	8
6.0	325	130	780	8	15	325	110	780	8
7.0	385	155	900	10	18	385	135	900	10
8.0	440	180	1,010	11	20	440	155	1,010	11
9.0	500	200	1,125	13	23	500	175	1,125	13
10	555	225	1,245	14	25	555	195	1,245	14
12	675	275	1,460	17	31	675	240	1,460	17
14	790	325	1,675	20	35	790	285	1,675	20
16	900	375	1,900	22	39	900	325	1,900	22
18	1,025	430	2,100	25	44	1,025	375	2,100	25
20	1,130	475	2,330	28	49	1,130	415	2,330	28

* Dosage of potassium in milliequivalents equals ml. KCl multiplied by 2.
† Figures for rate of administration are approximate and apply to both the dosage scales for correction of CO_2 of 5 mEq. and of 7.5 mEq. Rates in ml./hr. are readily calculated by multiplying drops/min. by the factor 4.

ing against the danger of hyperpotassemia by means of repeated electrocardiograms and, if necessary, chemical determinations of the level of potassium in the blood.

In Table 6 are found the requisite amounts of fluid for daily maintenance after the first 24 hours. The left half of the Table is designed to give the requirements for those patients who will be receiving parenteral fluids for periods up to four or five days. The right half of the Table specifies the amounts and kinds of fluids to be administered to patients requiring parenteral fluid therapy for prolonged periods or to patients whose state of nutrition is precarious. Although we have successfully employed the

TABLE 6.—*Therapy for Diarrheal Dehydration—Maintenance Schedules After First Twenty-Four Hours*

		Short-Term Therapy				Prolonged Parenteral Therapy			
Weight, Kg.	Average Surface Area, Sq. M.	Isotonic Saline, Ml.	5% Dextrose, Ml.	15% KCl, Ml.*	Rate, Drops/ Min.†	Plasma, Ml.	10% Dextrose, Ml.	15% KCl, Ml.*	Rate, Drops/ Min.†
2.0	0.14	30	225	2	3	50	370	2	4
2.5	0.16	30	260	2	3	60	420	2	5
3.0	0.19	40	305	3	4	70	500	2	6
3.5	0.21	40	335	3	4	75	550	2	7
4.0	0.23	45	370	4	4	85	605	3	7
4.5	0.25	50	400	4	5	90	655	3	8
5.0	0.27	55	430	4	5	100	710	3	9
5.5	0.29	60	465	4	6	105	760	3	9
6.0	0.31	60	495	5	6	110	815	4	10
7.0	0.35	70	560	5	7	125	920	4	11
8.0	0.38	75	610	6	7	135	1,000	4	12
9.0	0.42	85	670	6	8	150	1,100	5	13
10	0.46	90	735	7	9	165	1,210	5	14
12	0.52	105	830	8	10	185	1,365	6	16
14	0.58	115	930	9	11	210	1,525	7	18
16	0.65	130	1,040	10	12	235	1,710	8	20
18	0.70	140	1,120	11	13	250	1,840	8	22
20	0.77	155	1,230	12	15	275	2,020	9	24

* Dosage of potassium in milliequivalents equals ml. KCl multiplied by 2.
† Rates in ml./hr. are readily calculated by multiplying drops/min. by the factor 4.

long-term plan in a few patients for varying periods up to six weeks, our experience in this regard has been limited to the treatment of infants weighing less than 5 kg. However, the theoretical basis for extending the recommendations to larger children seems to be a valid one. One may add in this connection that the large requirement for protein in older children may be more suitably met by the use of solutions of amino acids rather than of plasma.

A few points which add to the usefulness and flexibility of the Tables may be mentioned. Under circumstances where laboratory data are not readily available the Reference Tables may nevertheless be applied by assuming, for an average case, that the dehydration has resulted in a loss of 10% of body weight and that the CO_2 combining power is 10 mEq. per liter.

It will be noted in Table 1 that blood (Fluid No. 2) is recommended for the therapy of obvious or suspected shock. In the treatment of patients admitted in a state of vascular collapse such that the delay entailed in preparation for transfusion may be hazardous it is advisable to alter the procedure to be followed. Plasma, which can be made immediately available, should be substituted for blood and administered as the initial fluid in amounts equal to those specified for the use of blood. Fluid Mixture No. 1 should then follow.

The schedules for the second and succeeding days (short-term therapy, Table 6) in the case of very small infants pose the technical difficulty of maintaining an extremely slow rate of drip in order to spread the restricted volume of fluid over a period of 24 hours. Even when the cut-down method of infusion is employed rates of flow of less than 5 drops per minute sometimes result in plugging of the needle. In some cases where it is desirable to continue intravenous therapy for a few days it may be advisable to augment the volume of 5% dextrose to correspond more nearly to that recommended in Table 6 for 10% dextrose under the plan for prolonged parenteral therapy. The more rapid rate of infusion thus made possible will help to insure continued patency of the needle.

An analysis of the data in the Reference Tables (1-6, inclusive) can be found in Table 7. Here for three representative weights, namely, 2, 10, and 20 kg., are listed the total fluids and electrolytes employed for correction of minimal and maximal degrees of dehydration and acidosis. Similarly tabulated are the ranges in composition of fluids recommended for maintenance. The figures represent the concentrations which would be present in each case if a single pooled solution were employed for a 24-hour period of treatment. It will be noted that during the first day the range of total fluids lies between

TABLE 7.—*Composition of Fluids Recommended in Reference Tables**

Wt. and Period of Treatment	Total Fluids Range, Ml./Kg.	Na Range, mEq./L.	K Range, mEq./L.†	Potential HCO_3 Range, mEq./L.	Cl Range, mEq./L.†
2 kg., 1st day	232-295	45-55	12-10	11-17	46-43
10 kg., 1st day	180-250	52-62	15-11	13-20	54-46
20 kg., 1st day	175-237	54-64	16-12	14-21	56-55
2 kg., maintenance	126-209	16-20	17-8	0-6	32-20
10 kg., maintenance	83-137	16-20	17-8	0-6	33-20
20 kg., maintenance	69-115	16-20	17-8	0-6	33-20

* Figures in mEq./liter represent concentrations which would be present in each case if a pooled solution of uniform composition were employed.

† The apparently reversed order of figures in these columns results from the fact that K, in contrast to the extracellular ions, Na and HCO_3, is administered in dosages which are independent of the severity of the diarrhea. The fixed amount of KCl employed thus accounts for higher concentrations of these ions when smaller volumes of total fluids are employed.

175 and 295 ml. per kilogram, whereas on subsequent days it lies between 69 and 209 ml. per kilogram. Likewise the sodium concentration varies from 45 to 64 mEq. per liter on the first day and from 16 to 20 mEq. per liter thereafter. The concentration of the electrolytes in the solution representative of the first day's treatment exhibits a range of 114 to 152 mOsm. per liter, or 38% to 51%, respectively, of the osmolarity of electrolytes in plasma. The corresponding figures for the fluids employed for maintenance are 56 to 66 mOsm. per liter, which are equivalent, respectively, to 19% to 22%

of that of the electrolytes of plasma. It may be of interest to point out also that the ratios of saline to lactate solution during the first day fall between a minimum of 2.3 : 1 (calculated for correction of the severest acidosis in the larger children) and a maximum of 3.7 : 1 (for correction of the mildest acidosis in a 2 kg. infant). It is thus evident that the standard 2 : 1 salt-lactate solution, if employed without modification, would provide lactate in excess of the maximal need as measured in the Reference Tables.

TECHNICAL ASPECTS OF INTRAVENOUS FLUID ADMINISTRATION

The apparatus used, as well as the method of control employed, in the administration of parenteral fluids is of paramount importance. The need for careful attention in this regard cannot be overstressed.

The apparatus (Fig. 1) consists of a 300 ml. calibrated Salvarsan burette connected to a drip chamber with a length of rubber tubing and then to a three-way stopcock with additional rubber tubing. The advantages of the Salvarsan burette are that fluids can readily be added and that the level of the fluid can be read with some accuracy. A 22 gauge hypodermic needle is used. For scalp veins a needle with a very short bevel is preferred. The cut-down method of inserting and securing the infusion needle in a vein is carried out only in the case of severely ill or moribund patients in vascular collapse and in the infrequent instances when it is impossible for a member of the house staff to insert a needle in a peripheral vein by simple puncture.

It is often difficult for the attending physician or house-staff officer to ascertain the status of the patient with respect to the fluids administered up to any given moment. Reference to the nurses' routine notes, where notations regarding fluids are interspersed with other bits of information, is usually unsatisfactory. It was found advantageous to devise a separate sheet for this purpose (Fig. 2). The sheet is fastened to the wall at the bedside of the patient who is receiving intravenously administered fluids. Spaces are provided for every hour of the day, and the sheet is changed daily. In the first column the nurse records the type and amount of each fluid that is added to the burette. In the next column the level of fluid in the burette is noted hourly. Following this the number of milliliters of fluid that have been infused during the previous hour are recorded. This is followed by a notation of the current rate of drip expressed in drops per minute. The nurse is required to initial the sheet each hour after having made entries in each of the columns. With the help of this system of notation one can tell at a glance exactly what fluids the patient has received, what fluid mixture is currently being employed, and whether it is being administered at the desired rate.

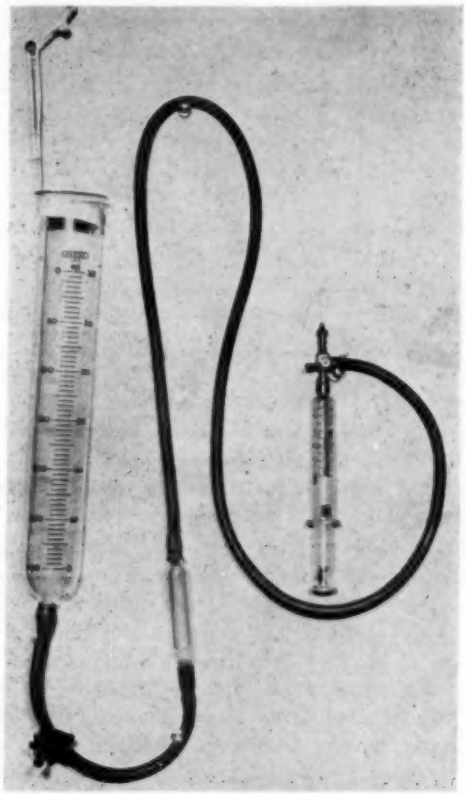

Fig. 1.—Apparatus employed for intravenous administration of fluids. Calibrations on the burette facilitate accurate supervision of the rate of infusion.

24 HOUR FLUID BALANCE SHEET

DATE June 4, 1954

NAME Johnny Doe AGE 2 mos. ROOM 410 UNIT NO. 423639

TIME	SOLUTION & AMOUNT, ml	FLUID LEVEL, ml.	ml./hr	DROPS/min	NURSE'S INITIALS
8 A.M.					
9 A.M.					
10 A.M.	First fluid mixture, 280 at 10 A.M.	280		31	A.T.
11 A.M.		160	120	21 15	A.T. A.T.
12 Noon		70	90	15	A.T.
1 P.M.	Blood, 95 at 1 P.M.	5 100	65	15	A.T. A.T.
2 P.M.	Final mixture, 200 at 2:40 P.M.	40 200	60	15 11	A.T. A.T.
3 P.M.		180	60	11	A.T.
4 P.M.	Final mixture-K, 20 at 4:10 P.M.	180 300	80	12	R.S. F.L.
5 P.M.		280	50	11	F.L.
6 P.M.		240	40	10	F.L.
		220	40	10	F.L.
7 A.M.					
8 A.M.		100	50	13	A.T.
Totals 24 hrs. ea. sol.	First fluid mixture, 280 Blood, 95 Final fluid mixture, 240 P.M.-8 A.M. 820				

Note 1. Start new sheet each morning.

2. Note initial solution and record routine readings each hour in space above dotted line

3. Note changes in solutions and adjustments in rates of flow in space below dotted line.

Fig. 2.—Bedside sheet employed for recording of fluids administered. The notations make it readily possible to ascertain what fluids and how much of each have been infused up to any given hour.

COMMENT

Rehydration of the extra- and intracellular compartments of the body during recovery from diarrheal disease is a complex process. It must take place concurrently with changes in the interrelationships of various ions in response to hormonal stress reactions, to correction of acidosis, and to replenishment of depleted stores of glycogen. No perfect therapeutic plan is at hand to guide one in the administration of precise amounts of cations, anions, dextrose, and water individually given at the specific rates required by each of the many reactions taking place. One can, however, after making a reasonably close clinical estimate of the nature and extent of the deficits, at least hope to arrive at a program which will permit the patient with a minimum of difficulty to make by himself the fine adjustments necessary for his recovery. Of crucial importance in such a program is the role which the kidney may be counted upon to perform. Without its capacity to conserve needed substances and to excrete superfluous or toxic accumulations of electrolyte and water the attainment of the exquisite balance found in health would be impossible.

Appreciation of the significance of renal function in facilitating the successful treatment of diarrheal dehydration has steadily grown since the original observations of Schloss [16] and the brilliant studies of Gamble.# Indeed, it has reached the point

References 17 and 18.

where some clinicians, a bit overawed by the remarkable powers of the kidney, deprecate their own ability to carry out therapeutic measures which can contribute materially to the patient's benefit. Despite the established practice of treating dietary or metabolic deficiency diseases by the specific administration of needed substances, these investigators appear to regard it as presumptuous to make similar efforts in the case of the deficiencies associated with disturbances of fluid balance. Instead they believe it to be better to confine themselves merely to recognizing that the patient is in need of fluids. Thereupon they favor the use, subject to renal approval or disapproval, of an "all-purpose" solution to be administered until the patient seems to be no longer in need of fluids.

TABLE 8.—*Electrolyte Composition of So-Called All-Purpose Solutions*

Solution No.	Na, mEq./L.	K, mEq./L.	Ca, mEq./L.	Mg, mEq./L.	Cl, mEq./L.	Potential HCO_3, mEq./L.	Potential HPO_4, mEq./L.
1	30	15	0	0	35	0	10
2	40	35	0	0	40	20	15
3	57	25	0	6	50	25	12.5
4	65	10	5	1	48	0	16
5	80	36	4.6	2.8	63	60	0
6	121	35	0	0	103	53	0
7	130	4	3	0	100	28	0
8	140	10	5	3	108	55	0

We have preferred not to embrace such a plan of treatment. If it is to be carried out it immediately gives rise to the question as to just what constitutes a satisfactory all-purpose solution. If one is to judge from the variety of commercially available solutions with multiple electrolyte content a ready answer is not forthcoming. In Table 8 there are listed a number of such solutions. Arranged in order of increasing sodium content, they exhibit a confusing variability in their content with respect to other ions. Comparison of the figures with those in Table 7 brings into sharper focus the magnitude of the problem of selecting a single solution which would be applicable under widely differing circumstances. Quite aside from this difficulty, however, there are other serious drawbacks which may be expected to result from the widespread use of all-purpose solutions. Of these perhaps the most unfortunate would come from discarding the practice of treating the patient in accordance with a careful assessment of his actual needs for reparative purposes as well as for daily maintenance. It may be anticipated that the complete reliance on renal homeostatic powers entailed in the employment of all-purpose solutions will be followed by failure of satisfactory management of cases presenting unsual aspects.

It is pertinent to point out, finally, that the use of a few simple solutions containing only sodium, potassium, chloride, and lactate ions affords the greatest flexibility in therapy. The addition of other ions, particularly calcium, may at times prove necessary. While convulsions occurring early in the course of diarrheal diseases are not usually due to tetany, some observers have noted hypocalcemia in the postacidotic phase of the illness.* We have not encountered the problem of hypocalcemic tetany in our patients and therefore do not consider a routine prophylactic addition of calcium ions necessary unless large amounts of phosphate are administered. The question of the appropriateness of phosphate ion added after reestablishment of renal function is still somewhat unsettled. Should such a change prove desirable it could be simply effected by the substitution for potassium chloride of a potassium solution of equal milliequivalence balanced in whole or in part by phosphate ions.

SUMMARY

A method of treatment of diarrheal dehydration is presented in which the details of fluid management are incorporated in reference tables.

The advantages of the method as well as the theoretical basis for the calculations employed are discussed.

For purposes of illustration the treatment of a hypothetical case is described.

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Hereditary Spherocytosis in a Negro Family

Report of Three Cases

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There are only 14 case reports of hereditary spherocytosis among American Negroes. We have recently had the opportunity of studying three Negro children with this disorder from the same family.

REPORT OF CASES

CASE 1.—On March 5, 1955, a 14-year-old Negro youth was seen for the first time in the accident room of Mercy Hospital. The patient was seen lying on the examining cot in an attitude of flexion on his left side and appeared acutely ill. His respirations were rapid and shallow, and he was unable to give an account of his present illness. The patient's mother and father supplied the necessary information, and stated that nine days previously the patient, who had been in good health, suddenly developed chills and fever. The patient's family physician was called. He examined the patient, stated that he had a viral infection, and prescribed an unknown medication. The patient was seen two days later by the family physician and given an injection of penicillin. The patient's symptoms continued, and the day before admission he complained of severe leg pain and became too weak to walk.

A review of the patient's family history revealed that his mother had been admitted to The Johns Hopkins Hospital in 1945 because of anemia and jaundice and had been splenectomized. His 13-year-old sister has epilepsy and is under treatment at The Johns Hopkins Epilepsy Clinic but was believed otherwise to be well. His older brother, aged 16 years, was believed to be entirely well. There were no other known familial diseases. The patient's past history revealed that he had been treated for pneumonia at the age of 2 years for a period of two weeks in the Baltimore City Hospital and that a blood transfusion had been given at that time.

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Physical examination revealed an acutely ill, dyspneic, and feverish, 14-year-old Negro boy, lying flexed on his left side. Rectal temperature was 102 F; pulse, 160; respirations, 40; blood pressure, 120/60. The patient's mucous membranes appeared pale, and the sclerae were icteric. An examination of the head and neck disclosed, in addition, a mild pharyngitis and moderate diffuse tender cervical adenopathy. An examination of the chest disclosed consolidation of the right lower lobe. The heart was found to be slightly enlarged to the left and a coarse systolic mitral murmur was heard. The liver was felt to be enlarged 2 fingerbreadths below the right costal margin, and the spleen was felt to be enlarged to 4 fingerbreadths below the left costal margin. The remainder of the physical examination was negative.

Blood was drawn immediately for culture and for hematologic examination. Hematocrit was found to be 12%, and the serum above the packed cells was seen to be very icteric. The mean corpuscular volume (MCV) was calculated to be 72 cu. μ and the mean corpuscular hemoglobin concentration (MCHC) 39%. Examination of the stained smear revealed a profusion of microspherocytes. A saline fragility test resulted in beginning hemolysis at 0.60% saline with complete hemolysis at 0.30% saline, while the control showed initial hemolysis at 0.45% saline and was complete at 0.20%. The white blood cell count was 46,600 and showed an extreme left shift with 1 blast cell, 7 neutrophilic myelocytes, 10 neutrophilic metamyelocytes, 22 staff neutrophiles, 49 polymorphonuclear neutrophiles, 6 lymphocytes, 2 monocytes, 2 erythroblasts, and 1 normoblast. Sickling test was negative. Hemoglobin electrophoresis disclosed only normal Type A hemoglobin. Reticulocytes were found to be 1.4%. Blood sugar and urea were within normal limits. The van den Bergh test showed 0.60 mg. direct bilirubin and 1.8 mg. indirect bilirubin per 100 cc. The serologic test for syphilis gave a weakly positive reaction when checked by the Kahn test and a negative reaction when checked by the VDRL test. The urine showed increased amounts of urobilinogen and no bile and was otherwise negative. The direct Coombs test was negative. The bone marrow obtained shortly after admission was found to be quite cellular but to have less than 6% erythroid elements and was interpreted as being compatible with bone marrow erythroid depression in an aregenerative crisis of congenital hemolytic jaundice.

The chest roentgenogram taken on the night of admission revealed an early pneumonic consolidation of the basal portion of the right lower lobe.

After initial examination in the accident department, 1000 cc. of 5% dextrose in normal saline containing 500 mg. of oxytetracycline (Terramycin) was started intravenously. After the absorption of 800 cc., the patient complained of shortness of breath and began to cough. Physical examination revealed early pulmonary edema, and prompt treatment was instituted, including rapid intravenous digitalization. The response to treatment was prompt, and 12 hours after admission the patient was cautiously transfused with whole blood, with further improvement. Transfusions were cautiously continued, and, under antibiotic therapy, the patient's pneumonitis and clinical condition showed steady improvement; on March 17, 1955, chest x-ray revealed the lung fields to be clear.

On March 26, 1955, a splenectomy was performed by Dr. William B. Rever Jr., and a 470 gm. spleen was removed. No accessary splenules could be found. No gallstones were palpable. Pathological examination showed the spleen to measure 14×10×6 cm., and on cross section the splenic pulp was bloody red but firm. Microscopic examination showed the general architecture of the spleen to be well preserved. The pulp substance contained many thick-walled sinuses. The endothelial linings were hyperplastic. The Malpighian corpuscles were widely separated but appeared normal. These findings were believed to be compatible with the spleen in congenital spherocytic hemolytic anemia.

The patient's postoperative course was uneventful, and he was discharged from the hospital on April 4, 1955, and was followed in the medical and surgical outpatient departments. Examination of the peripheral blood before discharge showed 14.3 gm. of hemoglobin and a 46% hematocrit with 2.8% reticulocytes. On April 22, 1955, in the outpatient department, the patient was found to have 16.0 gm. of hemoglobin per 100 cc. with 5,560,000 red cells and a hematocrit of 50% and to be feeling well.

At the time of the patient's original admission into the hospital, his parents were advised that a complete family study should be carried out to determine if the patient's brother or sister or relatives had the same condition. March 9, four days after the patient's admission, the parents presented themselves and the brother and sister for examination. The patient's father was found to have a hematocrit of 53%. No spherocytosis could be detected on examination of his stained blood smear. His red cells did not sickle. The patient's mother had a hematocrit of 39%, and examination of her stained smear showed a profusion of microspherocytes. The patient's sister, 13 years of age, was seen to be moderately jaundiced and anemic. Her physical development appeared moderately retarded. Her hematocrit was 27.5%, and examination of her abdomen revealed a palpable spleen, 3 fingerbreadths below the left costal margin. Her stained smear revealed a profusion of microspherocytes. A saline fragility test carried out with this blood revealed initial hemolysis at 0.65% saline and complete hemolysis at 0.30% saline, while the control blood showed initial hemolysis at 0.40% saline and complete hemolysis at 0.30% saline. The patient's older brother, aged 16 years, appeared to be moderately jaundiced, but anemia was not evident. An examination of his abdomen revealed the spleen to be barely palpable at the left costal margin. Microspherocytosis was quite evident in his blood. His hematocrit was 46%. A saline fragility test carried out with this blood resulted in initial hemolysis at 0.60% saline and complete hemolysis at 0.30% saline, with the control blood showing initial hemolysis at 0.40% saline and complete hemolysis at 0.30% saline.

It was thus apparent that both the patient's brother and sister had hereditary spherocytosis, and the parents were so advised. Repeated attempts to have the mother's two sisters and brother come in for hematologic examinations were unsuccessful.

CASE 2.—Three days following this examination the patient's 13-year-old sister developed severe frontal headache, and the following day her temperature rose to 102 F and she became nauseated. The following day she developed severe pain in the left upper quadrant of her abdomen and became very weak. Her parents noticed that her hands were extremely pale and that she was becoming lethargic and brought the patient to the accident department for treatment.

A review of the past history of the patient revealed that she had epilepsy of five years' duration and was under treatment at The Johns Hopkins Epilepsy Clinic with primidone (Mysoline).

Physical examination revealed a pale, lethargic, poorly developed, Negro girl, aged 13 years, appearing acutely and chronically ill. Blood pressure was 110/60; pulse, 120; respirations, 20. There was moderate cervical lymphadenopathy. There was a sinus tachycardia with a Grade 2 mitral and aortic murmur which was transmitted upward into the carotid vessels. The lungs were clear. The liver was not palpable. The tip of the spleen was barely palpable under the left subcostal margin. There was bilateral costovertebral angle tenderness.

The peripheral blood on admission showed 5.7 gm. per 100 cc. of hemoglobin, 2,200,000 red cells, and a hematocrit of 18%. The MCV was 81 and the MCHC 32%. The reticulocyte count was 1.2%. The saline fragility test was not repeated. The white blood cell count was 8,900, with 1% staff neutrophiles, 64% segmented neutrophiles, 33% lymphocytes, and 2% monocytes. The van den Bergh test showed 0.4 mg. per 100 cc. direct bilirubin and 0.9

mg. indirect bilirubin. Platelets numbered 230,000 per cubic millimeter. The blood sugar and blood urea were within normal limits. Urinalysis was negative.

Chest x-ray on the day of admission was clear.

The patient was given 250 mg. of tetracycline every 6 hours by mouth and 800,000 units of penicillin procaine intramuscularly every 12 hours, with the result that there was rapid clinical improvement and the patient was afebrile on the sixth hospital day and remained afebrile until the time of surgery. One pint of whole blood was given on the second, the fourth, and the sixth hospital days, with a gradual rise in hemoglobin to 14.2 gm. on the day prior to surgery.

On the 13th hospital day a splenectomy was performed by Dr. William B. Rever Jr. under endotrachial anesthesia. The spleen weighed 230 gm. No gallstones were palpable. Microscopic section of the spleen showed the capsular and trabecular elements intact. The pulp was relatively acellular, and its bulk was made up of sinuses with hyperplastic linings. The Malpighian bodies were intact but were widely separated and relatively hypoplastic. There was some pigmentation in the reticulum of the pulp. The microscopic picture was rather nonspecific but considered to be compatible with congenital spherocytic hemolytic anemia.

The patient's postoperative course was complicated by a number of brief convulsive seizures, during which time there was twitching of both arms and legs and the patient would void involuntarily and stare off into space. The seizures each lasted from one to three minutes and occurred several times on the first postoperative day, despite medication with primidone and mephobarbital (Mebaral). After the first postoperative day the patient continued to improve, and the remainder of the postoperative course was uneventful. The patient was discharged on the 22d hospital day to be followed in the outpatient department. On April 22, 1955, in the outpatient department, the patient's hemoglobin was 14.3 gm. per 100 cc., hematocrit 47% and red cell count 5,220,000. She has been followed in The Johns Hopkins Epilepsy Clinic on primidone and diphenylhydantoin (Dilantin) therapy and has experienced only a few seizures, lasting about a minute each, since discharge, according to verbal reports from the mother.

CASE 3.—The 16-year-old brother of the first patient, in the family group, had been found to have hereditary spherocytosis when initially examined as an outpatient on March 9, 1955. His hematocrit at that time was 46%, and moderate jaundice was evident. He appeared at that time to be in good health. He continued feeling well, following this examination, until March 14, 1955, when, while in school, he became suddenly dizzy and developed a throbbing headache. His temperature at that time was found to be 101 F. The following day the headache subsided and he began to experience a watery diarrhea with moderate, colicky, periumbilical pain. He was seen in the accident department on March 16, 1955, and was thought to have mild gastroenteritis and was given a medication and discharged. The following day he returned for reexamination and was found to be quite pale. His hematocrit was 30% and reticulocytes were 1.2%. It was felt at this time that the patient was experiencing an aregenerative crisis in congenital spherocytic anemia, and he was admitted for observation. Physical examination on the day of admission disclosed a well-developed, well-nourished, Negro boy 16 years of age, appearing pale but not acutely ill. Positive findings on physical examination were pallor of the mucous membranes and nail beds, moderate anterior cervical lymphadenopathy, and a Grade 2 blowing systolic heart murmur that was heard in the mitral area. The spleen could not be felt at this time.

Hematologic examination disclosed 10.0 gm. per 100 cc. of hemoglobin, 4,200,000 red cells per cubic millimeter, hematocrit 30% with an MCV of 72 and an MCHC of 30%. Reticulocytes numbered 1.2%. The white blood cell count was 10,000, with 4% staff eosinophiles. The platelet count was 230,000 per cubic millimeter.

Blood chemical examination disclosed a normal sugar and urea and 4.1 mg. per 100 cc. of total bilirubin, with 0.4 mg. direct bilirubin. The chest x-ray was interpreted to be within normal limits.

The patient was given tetracycline (Panmycin) by mouth and transfusion of whole blood. On April 25, 1955, a splenectomy and an appendectomy were performed by Dr. William B. Rever Jr., under endotracheal anesthesia. The spleen weighed 500 gm. Three small accessory spleens were also found and removed. The spleen measured 17×12×6 cm. and had a dull purple capsule. Cross section of this organ showed a dark red spongy stroma. Microscopic examination showed the trabeculae and Malpighian bodies to be relatively deficient. The pulp was engorged, and the sinusoids were conspicuous. The general architecture was preserved. The accessory spleens were 0.3 to 0.5 cm. in diameter and disclosed a similar microscopic pattern. One of the accessory spleens was partially calcified. No gallstones were palpable. The appendix was found to have a small granulomatous nodule at the tip. Microscopic sections identified this lesion as a foreign-body granuloma. The patient's postoperative course was uncomplicated, and he was discharged on the 18th hospital day to be followed in the outpatient department. On April 22, 1955, his hemoglobin was found to be 16.2 gm. per 100 cc., hematocrit 51%, and red cell count 5,670,000, and he felt entirely well.

Comment.—Following the discharge of these patients, we were informed by Dr. C. Lockard Conley, at The Johns Hopkins Hospital, that a search of their records disclosed that the mother of our three patients was the single Negro patient with hereditary spherocytosis, seen by Dr. Wintrobe, and mentioned in his book, "Clinical Hematology," as a case in a Negro of obviously mixed blood. It is not apparent on examination of our three cases that there is an admixture of blood, but the mother is brown-skinned and has freckles and facial characteristics that support the probability of a mixed genealogy.

COMMENT

Temporary suppression of erythocyte production is a well-known accompaniment to many types of acute infectious disease. When this process involves hematopoeisis in an individual with red cells of normal life span of about 120 days, there is little change in the hemoglobin level of the blood, and after a few days erythropoiesis recovers in the marrow and little damage results. When the same process occurs in patients with red blood cells of short life span, such as those in sickle-cell anemia, hereditary spherocytosis, and acquired hemolytic anemia, the results may be disastrous. When the source of replenishment of red cells is inhibited by infection, anemia may rapidly ensue and may reach sufficiently low levels as to cause congestive heart failure and death if no treatment is available. This process was well illustrated in our first patient, who when first seen was found to have a hematocrit of 12% and who developed pulmonary edema shortly after intravenous fluids containing antibiotics were started. Prompt intravenous digitalization and other measures restored cardiac reserve to the point that transfusions with whole blood could be carried out without further congestive failure.

Gänsslen, Zipperlen, and Schüz (1925) emphasized the association between hereditary spherocytosis and other congenital abnormalities, such as tower skull, brachycephaly, eye abnormalities, polydactyly, brachydactyly, and infantilism. We noted moderate tower type skulls in the two male patients, Cases 1 and 3, and obtained x-rays of the skulls. The skull x-ray of Case 1 was read as "The AP diameter of the skull is rather short, and the height appears increased. The patient's facies are of the prognathous type. There is no evidence of thickening of the diploe or other significant abnormalities." The skull x-ray of Case 3 was read as normal.

SUMMARY

Three new cases of hereditary spherocytosis in a Negro family are presented. Each patient in this series presented with the sudden development of anemia due to an aregenerative erythroid crisis probably due to a viral agent.

Hereditary spherocytosis should be considered in the work-up of Negro patients with hemolytic disease even if sickling or abnormal hemoglobins are demonstrated.

The spleen may not be palpable in a patient with hereditary spherocytosis in an aregenerative crisis.

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Special Articles

A HISTORY OF CHILDREN'S HOSPITALS

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IN A STRICTLY modern sense, children's hospitals are usually considered to be institutions that limit themselves to the care of sick children. This concept, however, is not wholly true. A number of the larger children's hospitals have included within the sphere of their activities not only treatment but preventive care as well and have always emphasized research and teaching. Some, like the Children's Hospital of Philadelphia, have evolved into great children's medical centers covering nearly every phase of child welfare and study.

The history of children's hospitals is, of course, closely linked with the history of hospitals in general. Embryonic types of hospitals are known to have existed in the early civilizations of Mesopotamia, Egypt, Asia, and other areas. Ceylon had a hospital in the fifth and another in the second century B. C.; eighteen physicians worked in the latter hospital. In India, King Asoka established hospitals in the third century B. C., and there were ancient hospitals in Siam and Persia.

In Ireland, where the Druids had physicians, there was a "House of Sorrow" as early as 300 B. C., and the Brehon Law from about the fifth century A. D. made frequent references to hospitals, as it did also to the education and foster care of children.

It is more than likely that in all these hospitals children were frequently cared for on one basis or another. There is ample evidence that children, as well as adults, were treated in the great Greek temples of healing which go back at least to the fifth century B. C.

Outpatient dispensaries are likewise of ancient lineage. In a way, the Babylonian custom of bringing the sick to the market places or the gates of the city for consultations with passers-by was a form of outpatient practice. The ancient Egyptians had state physicians to attend the sick poor, and the public dispensaries of Athens, called iatreia and mentioned by Pindar and Plato in the fifth and fourth centuries B. C., were apparently carried over into classical Rome as the tabernae medicae. The archiatri populares in the time of Hadrian were medical officers whose work was probably confined to treatment of outpatients.

Various institutions of healing, such as the iatreia, the Asclepieia, and the valetudinaria, continued to exist throughout the Roman Empire well into early Christian times. With the rise of Christianity early in the fourth century A. D., a system of public hospitals was organized to replace the earlier pagan institutions. In A. D. 325 at the Council of Nicaea, regulations were adopted for hospitals, foundling homes, and asylums for children, and it was decreed that in each Christian village there should be established a xenodochium to assist pilgrims, the sick, and the poor, including children.

In ancient times, children, particularly deformed ones or females, were often unwanted, and infanticide was condoned. When orphans, foundlings, or other undesired children were not murdered, it was a common practice to abandon them. Certain spots became especially popular for the so-called exposure of infants, such as the Cynosarges, an academic gathering place near Athens, or the Colonna Lactaria in the Forum Olitorium, a vegetable market place in Rome, where wet nurses were wont to convene in

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order to sell their breast milk to mothers who needed it. If these babies were picked up, they could be raised as the slaves of their "rescuers."

Ovid and many other writers during the centuries that followed called attention to this practice, bewailing the fate of such exposed children.

Christianity frowned upon this custom and eventually drew up laws against the practice, but when it became illegal to enslave these children, they practically all perished. It was, therefore, necessary to adopt some measures that might save them. There were already in existence institutions known as brephotrophia, which were homes or asylums where infants were received and nursed, and orphanotrophia for orphaned and older children, but these were totally inadequate to meet the needs of the Dark Ages.

In A. D. 364, a school was organized at Edessa where St. Ephraem built a hospital which was used in the clinical instruction of medical students. Here the Nestorians flourished for over a century until they were driven out. They then established themselves in Persia, founding schools and hospitals, the most famous of all being set up at Gondisapor. This school thrived from about A. D. 530 until at least the end of the tenth century and became the greatest intellectual center of that era. The famous hospital here, the Bimaristan, became the prototype for all the subsequent hospitals which the Arabs founded in Baghdad, Damascus, Cairo, Cordova, and elsewhere.

In A. D. 369, St. Basil built his great hospital at Caesarea, which likewise became a model institution for others that were called Basilias and established in many parishes in conjunction with the churches.

In these, foundlings and children were also cared for. The early Christian deaconesses, forerunners of the later nuns, in addition to practicing a sort of "district nursing," set up hostels for patients which became known as diakonias. In A. D. 380, the famous hospital sponsored by Fabiola was built at Rome, which was really the first to limit itself to the care of the sick. St. Jerome called it a nosocomium and stated that Pammachus, a Roman Senator, a little later founded a xenodochium. In the fifth century, Pope Symmachus built hospitals in connection with the three great churches of Rome, St. Peter's, St. Paul's, and St. Lawrence's, and shortly after the middle of the sixth century, Belisarius founded a xenodochium in Rome.

In the ninth century, Soror opened a great hospital at Siena and established a nursing order in conjunction with it which became a model for future similar nursing orders. Bartolo's frescoes on the walls of the hospital of Siena tell the story of the work that was done for foundlings and pilgrims, as well as for the sick, in its early days. Probably the masterpiece of the old painters in this hospital is the "Stair to Heaven" by Vecchietta, which was evidently painted for the department of foundlings. Its subject is the ascent of these little children to heaven and their welcome by the angels, the saints, and the Heavenly Father. Too often, it seems, the devout attendants of these children were more carried away by this aspect of their work than by their zeal for the physical well-being of their little charges.

The Arabs of the early Moslem period likewise had a highly organized system of hospitals, orphanages, and other asylums which became active medical centers. Such a hospital was founded in 707. Another, erected in 1283, had an orphanage associated with it, and home care was furnished when required.

The great Rhazes from his extensive practice in Persian hospitals was able to write profusely, giving us clear clinical pictures of diseases; much of his writing pertains to children. Indeed, he was the first medical author to devote an entire treatise to the diseases of children. He enjoined the student of medicine to attend the hospitals constantly and, in company with the most acute professors, to pay unremitting attention to the conditions of the inmates.

Care of the newborn must have been an important feature, also, in the various hospitals that were founded for maternity cases, such as the one established by Wenzel III

in Prague in 928 and the one founded at Esslingen in Germany in 1233.

FOUNDLING HOMES

One of the early phases of social welfare in childhood was the foundling house. Since this type of institution was for centuries the only place in which children received care, it was here that clinical pediatrics really developed. These foundling houses were the precursors of the modern children's hospitals, but a long road had to be traveled before sick children were segregated into the children's hospitals of our times. These homes were veritable charnel houses for infants and did little to reduce the infant mortality rate, even for abandoned children, whose fate was hardly improved by them. The best that could usually be offered was spiritual salvation, because for nearly two thousand years the death rate approached the 100% mark.

At first, the Church undertook to salvage infant outcasts. The Council of Vaison in 442 provided that an abandoned child should find sanctuary in a church for ten days. This was repeatedly confirmed by subsequent councils. Mothers who were previously driven to expose their infants could now leave them in a marble receptacle which was placed at the church door. Wet nurses were obtained for these children; they were cared for to the age of eight years and freed from slavery, and not infrequently adoptive parents were secured.

The first modern foundling asylum was established at Milan in 787 by Archbishop Datheus. Similar institutions followed during the subsequent centuries. The architecture of the Hospital of the Innocents, as the foundling house of Florence was called, was the work of Brunelleschi, and the loggia is adorned with a series of medallions by Della Robbia depicting infants in the swaddling clothes of the medieval period, portraits which have become the symbol of pediatrics.

At the Conservatorio della Ruota, a foundling home established in Rome in conjunction with the Ospedale della Santo Spirito by Innocent III with accommodations for 600 foundlings, appeared for the first time the *ruota,* a revolving cradle which enabled the anonymity of the child to be preserved when it was received at the gate. Ever since, this has remained a requisite of foundling homes. In Germany it was called a *Torno* or *Drehlade* and in France, *le tour.*

In the thirteenth century, many monasteries were built to which were attached foundling asylums that were served, if possible, by a physician and a surgeon from among the monks. The children brought to these foundling institutions were nursed by women, each woman, as a rule, being assigned the care of six children.

Among the Aztecs of Mexico, the Spaniards found an extraordinary hospital system fully developed upon their arrival in the New World. Every town contained at least one hospital for the care of the sick. Each was amply endowed and attended by physicians who were in many ways superior in medical knowledge to the average practitioner of fifteenth-century Europe. The Mayas and the Incas also had orphan asylums before the coming of the Europeans, but little is known about them except that they were suppressed and replaced by the Church institutions.

The first hospital in the New World operated by Europeans was probably founded at Santo Domingo in 1503. In 1532, Pedro de Gante, a great Spanish philanthropist, already had 500 or 600 children under his charge in a large school in Mexico to which was also attached, of necessity, a hospital. Another great benefactor was Vasco de Quiroga, who, among his many philanthropies, established an institution near Mexico City about 1563 which included a hospital with wards for children and a foundling home where wet nurses were employed.

Abandoned children were also plentiful in Peru. Father Luis Ojeda, moved by the sight of a pack of dogs devouring such an exposed infant in a street in Lima, organized in that city in 1597 a foundling home with a ward for sick infants and with wet nurses to care for the babies. During the

next century, foundling homes were established in Bogota, Pernambuco, and Rio de Janeiro.

The great Foundling Asylum of Mexico City, affectionately called "La Cuna," was established on Jan. 11, 1767, and the detailed regulations were reprinted not so long ago by Leon.

The Foundling Hospital of Paris was founded in 1636. Originally known as "La Couche," it was taken over by St. Vincent de Paul in 1640; its name was changed to Hôpital des enfans trouvés, and many improvements were made in its management. In 1670, it was placed under government control and has ever since headed the extensive system of infant welfare in France. It was in this institution that Billard, in the early part of the nineteenth century, performed the studies that led to his treatise on "Diseases of Infants." These studies were instigated by the complaint of Morgagni that little was known of the pathology of infancy, and Billard carried out clinical observations and correlated them with postmortem findings. This was the first book of its kind and set the style for pediatric textbooks for the next hundred years.

In Ireland, a workhouse and foundling asylum were founded at Dublin in 1702. The Foundling Hospital of London, made famous by many great writers and artists of the eighteenth century who espoused the cause of neglected children, was established in 1739. In all these institutions, the failure to reduce the mortality rate among children appalled everyone concerned.

In 1754, William Cadogan became physician to the Foundling Hospital of London, and by 1768 his "Essay upon the Nursing and the Management of Children," originally written in 1748, had had many good effects, not the least of which was the discontinuance of the universal practice of swaddling infants.

CHILDREN'S HOSPITALS

There were no hospitals limited to the care of sick children before the nineteenth century. Until then, children, when treated at all, were indiscriminately treated along with adults in general hospitals. When a nursing mother had to be admitted to a hospital, she was as likely as not to bring her baby along with her. If there was a foundling home associated with the hospital, very young infants might be transferred there. These young infants were not wanted by the general hospitals, as a rule. Physicians, nurses, attendants, all felt frustrated with their lack of success in treatment. Even after children's hospitals were established, infants under two years of age were seldom accepted because the high death rate alarmed the hospital management. The Massachusetts General Hospital cared for children from the time it was opened in 1811, but they were treated with adults both in the hospital and as outpatients. Many were very young, their mothers remaining with them. A separate children's department was not established until 1910.

The movement for separate hospitals for sick children had its real beginning in the second half of the eighteenth century, when, in 1769, George Armstrong opened his Dispensary for the Infant Poor in London. The idea had been germinating in the minds of many, but Armstrong, outlining the many reasons for his belief that inpatient care for young infants was impractical, firmly held that dispensary treatment was the ideal way to meet the needs of sick children. He labored hard and valiantly to maintain his clinic, often seeing more than sixty patients a day, but was unable to enlist effective support and finally succumbed under the financial and physical strain of his noble effort.

At this dispensary, teaching was carried out, mothers were instructed in the care of well babies, and annual reports and an excellent "Essay on the Diseases Most Fatal to Infants," which included "Rules in the Nursing of Children with a Particular View to Those Who Are Brought Up by Hand," went far to persuade other practitioners to attend children.

The second such dispensary, organized in Austria in 1787 by Joseph J. Mastalier, was the First Public Institution for Sick Chil-

dren, better known as the Vienna Clinic; it was more fortunate and has survived to the present day. Beginning as a modest project, it became the cradle of Austrian pediatrics, where preeminent specialists attracted students from everywhere.

The first modern hospital confined to the care of sick children was the Hôpital des enfants malades of Paris which was established by the French government in 1802. At the end of the eighteenth century, hospitals in general were in a deplorable condition; with few exceptions they were loathsome institutions, breeders of pestilence, and as much feared by the sick as they were repugnant to the senses of sight and smell of the healthy. In 1785, King Louis XVI of France ordered an investigation of the Hôtel Dieu of Paris. The investigators, among whom were outstanding members of the medical profession led by Tenon, as well as famous scientists like Laplace and Lavoisier, saw a hundred or more patients penned in a ward. Often eight or nine children were heaped in a single bed. Measles, smallpox, malignant diarrheas, and scabies were crowded together in each bed, children and adults in the same overcrowded ward. The report established two essential points: (1) that each patient should have an individual bed, and (2) that the children should be separated from adults.

The Hôpital des enfants malades was opened in the tenth year of the French Republic as a three-hundred bed hospital. Children between the ages of two and fifteen years with every kind of acute and most of the chronic diseases were admitted. The contagious disease wards were separated from the rest of the hospital by large gardens and courtyards. Yet even here, the original warnings against commingling contagious diseases were soon forgotten. By 1876, bed after bed was occupied with recognized cases of measles, scarlet fever, diphtheria, typhus, pneumonia, and tuberculosis. Similar conditions seem to have prevailed elsewhere. It was not until the end of the nineteenth century, when the bacteriological differentiation of disease was clearly defined and the antiseptic era well on its way, that separate institutions were provided for contagious diseases, and these were then excluded from the general hospitals.

The Hôpital des enfants malades, still the oldest and largest children's hospital of Europe, soon became an investigating and teaching center where specialists such as Jadelot, Guersant, Trousseau, and Bouchut attracted physicians from all over the world and published the results of their experiences in pediatric texts that were widely used. Probably the most important book originating here was the monumental three-volume work by Barthez and Rilliet in 1838 to 1843 that became the Bible of pediatricians for many years.

More than three decades elapsed before other children's hospitals began to appear. In 1834, through the efforts of Dr. Friedeburg, the Nikolai Hospital for Children of St. Petersburg was founded in Russia. Starting with sixty beds as a voluntary hospital with only meager support from the government, this was the second hospital for sick children in Europe. The third was St. Anne's Children's Hospital of Vienna, which opened in 1837 with twelve beds, and which soon, in conjunction with the Vienna Clinic and the Imperial Foundling House of Vienna, became an active seat of clinical research and teaching that likewise attracted many students from all the world. Children's hospitals then sprang up rapidly throughout continental Europe: in Hungary in 1839, and during the next decade at Hamburg, Stuttgart, Ludwigsburg, and Prague. Then second ones were founded in Vienna, St. Petersburg, and Moscow, two in Turin, two in Berlin, others in Graz, Frankfurt-am-Main, Lemberg, Munich, Brünn, Cassell, and Bremen.

In England there was no hospital for children until 1852, when The Hospital for Sick Children in Great Ormond Street, London, was founded by Dr. Charles West, who, having previously conducted the Royal Infirmary for Children in London, persisted in the idea of a hospital for inpatients until success finally crowned his efforts. A house

at 49 Great Ormond Street, which had once been the residence of the famous Dr. Richard Mead, was rented and furnished to accommodate ten patients. Soon the ten beds became twenty, and before the end of the year the physicians were asking, as they still are today, for more beds. A special "fever ward" was provided for contagious cases, but smallpox was excluded. There was one nurse in charge. An autopsy room for the study of disease was provided, and the dispensary, as with nearly all other such hospitals, became a busy and important adjunct. Teaching of nurses, medical students, and practitioners, as well as instruction of the public in the management of children, was instituted from the beginning. Among some of the great pediatric teachers there whom we might single out for mention were West, William Jenner, Gee, Cheadle, Barlow, Poynton, and Still.

In the United States the Children's Hospital of Philadelphia was the first such hospital to be opened. It was established in 1855 and is this year celebrating its centennial. Fathered by the Pennsylvania Hospital, which itself was the first hospital of its kind in the United States, the Children's Hospital of Philadelphia was also largely influenced in its origin by Great Ormond Street Hospital of London and the Hôpital des enfants malades of Paris. It was founded for the children of the poor, with twelve beds for patients up to twelve years of age suffering from noncontagious diseases and accidents. The founders, by providing an example of good medical care, as well as a place for the study of children and the dissemination of medical knowledge thus gained, hoped to cut down much of the mortality then prevailing among children. An outdoor dispensary was set up and even home care furnished. The hospital has made two major moves during its hundred-year lifetime—the first in 1867 and the second in 1916 to its present site, where it has continued to grow and develop into today's Children's Medical Center, with not only many divisions and departments for treatment, education, and research, but with affiliate and cooperative arrangements with many outside agencies concerned with child welfare.

Among the pioneers of American pediatrics who have been associated with the Children's Hospital, space permits mention of only a few: John Forsyth Meigs, Louis Starr, John P. C. Griffith, Alfred Hand, John Gittings, A. Graeme Mitchell, Howard C. Carpenter, all of particular pride to us in Philadelphia.

The Children's Hospital of Boston was the second children's hospital in this country, established in 1869 with twenty beds. Other major children's hospitals were founded at Washington, D. C., and New York in 1870; Albany, San Francisco, and Toronto, Canada in 1875; Detroit in 1877, and St. Louis in 1879. The Royal Alexandra Hospital for Children of Sydney, Australia, was founded in 1880.

7043 Elmwood Ave. (42).

Case Reports

CUSHING'S SYNDROME

Report of a Case in an Infant Twelve Weeks Old

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and
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CUSHING'S syndrome is rather rare in infants.* In 1949 Chute, Robinson, and Donohue collected from the literature 32 cases of Cushing's syndrome in children and added 1 case of their own.[1] Because of differences of opinion about the criteria of Cushing's syndrome, some cases have been recorded under other titles. For instance, in 1940 Marks, Thomas, and Warkany collected a series of cases of adrenocortical obesity in children, some of which apparently were examples of Cushing's syndrome.[5]

Cushing's disease is the term that has been suggested for the cases in which the classical clinical features described by Cushing are associated with a basophilic adenoma of the pituitary.[6] The name Cushing's syndrome is applied in those cases where causes other than basophilic adenoma are found. It is now generally accepted that the syndrome is usually associated with an adrenal cortical tumor or hyperfunction of the adrenal cortex.[6] Indeed, most of the features of Cushing's syndrome may be produced by administration of cortisone over long periods of time.

The following case occurred in a baby 12 weeks old. We believe this is the youngest infant on record with a full-blown Cushing's syndrome.

REPORT OF CASE

A girl 2 months 25 days of age was admitted to The Memorial Hospital on Dec. 31, 1954, in coma.

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From The Departments of Pathology and Pediatrics, The Memorial Hospital.

* References 1 and 5.

Past History.—The child was delivered by low forceps on Oct. 6, 1954, to a healthy, normal 26-year-old primipara. The mother was at term and had gained 30¼ lb. At birth, the child weighed 11 lb. 4½ oz.; it cried spontaneously.

The child was seen by a physician at one month of age for a well-baby check up. She weighed 11 lb. 14 oz. The eyes appeared slanted and the tongue protruded. Her weight gain was considered poor. She was seen again at 2 months of age; this time she weighed 14 lb. 10 oz. The slant-eyed appearance and protruding tongue were still noted. The parents were told that the child might not be normal and should be observed. The possibility of Mongolism was considered.

On Dec. 20, 1954, at the age of 2 months 14 days, the child was seen by a second physician who reported a very obese child with marked hypotonia. She weighed 15 lb., had eczema of the face and erythema of the buttocks, and the liver border was palpable 2 cm. below the costal margin. Further evaluation was deferred to permit the child's development to be watched.

The child was again seen on Dec. 26, at the age of 2 months 20 days, for a "cold". She weighed 15 lb. 8 oz. Otherwise, the physical findings were the same as before.

Present Illness.—On the evening of Dec. 30, the child was given 3 to 4 drops of camphorated opium tincture because of irritability. The next morning she was apparently well until after feeding, when she suddenly became comatose and cyanotic. The parents also noticed a reddish spot on the back. The child was admitted to the hospital and placed in an oxygen tent.

Physical Examination.—The temperature was 102 F, pulse rate 100, and respirations 40. The child was comatose and did not respond to stimuli. The child was obese; her eyes were Mongoloid in appearance, the pupils were of pinpoint size and did not react to light. The nape of the neck was large; the cheeks, large; the nose and throat, negative, and the chest, clear. The toes and fingers were described as stubby. There was a soft systolic murmur at the apex. Below the spleen, in the left flank, a firm mass was felt by two observers. The possibilitiy of intussusception was suggested by one observer. The possibility of poisoning from the opium tincture also was considered.

Course in Hospital.—X-rays of the head and body revealed nothing abnormal; laboratory studies

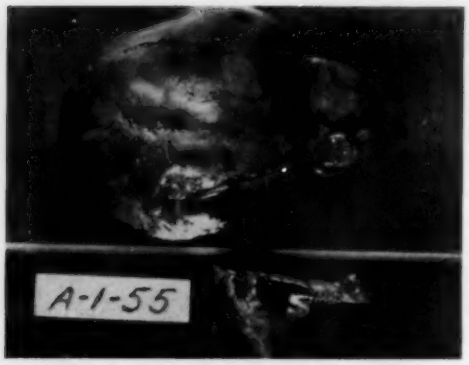

Fig. 1.—Gross photograph of both adrenal adenomas. Upper figure, left adrenal, external surface; lower figure, cross section of right adrenal showing small tumor (dark area) in cortex.

were not made, and no blood pressure was recorded. Despite oxygen, stimulants, and penicillin, the child remained in coma and her temperature rose to 106 F the day after admission. She died 35 hours after admission.

Autopsy Findings.—Gross Examination: The body was that of an obese girl 2 months 25 days old, weighing 15 lb. and measuring 24 in. in length. There were large fat pads on the cheeks and on the nape of the neck, but fat was also generously distributed over all parts of the body. The face showed an aciniform dermatitis. The external genitalia appeared normal. There were no teeth.

The body cavities were lined with smooth glistening membranes. The heart was enlarged and weighed 45 gm. The left ventricle was greatly hypertrophied; the right ventricle, moderately so. The valves, coronary vessels, endocardium, and epicardium appeared normal. No abnormalities were observed in the large vessels. The lungs showed moderate congestion. The left kidney weighed 28 gm. and was indented in its upper pole by the overlying adrenal mass. The right kidney was not remarkable.

The left adrenal gland was replaced by a large nodular encapsulated tumor, which measured 6×4×3 cm. and weighed 35 gm. On section, the tumor tissue was various shades of brown and was noted to be friable, soft, focally necrotic, and hemorrhagic. The right adrenal gland weighed 6 gm. and had a partly swollen central portion occupied by a tumor-like mass of fusiform shape lying in the long axis of the gland. On section, this tumor mass was dark reddish brown and stood out clearly from the surrounding adrenal cortex.

Fig. 2.—Postmortem photograph of the patient. Note obesity, fat cheek pads, and peculiar appearance of eyelids. Age: 2 mo. 25 days.

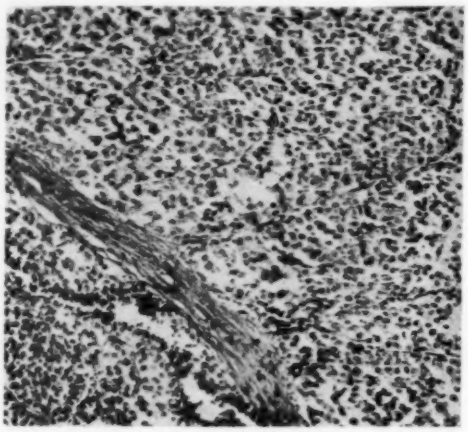

Fig. 5.—Photomicrograph of the large adrenal cortex adenoma (left). Note the regular cords of cells. × 100.

The brain weighed 420 gm. There was some congestion of the meninges in the occipital region. Cutting through the brain stem disclosed a large hemorrhage involving the entire central area of the pons and extending anteriorly. This hemorrhage was about 2 cm. in diameter and had destroyed a rather large amount of the brain parenchyma in this region. The blood did not escape into the ventricles or into the subarachnoid space. The pituitary gland and other remaining organs were apparently normal grossly.

Microscopic Examination: Heart. Sections of the left ventricle showed hypertrophy of individual muscle fibers.

Adrenal Glands. The left adrenal gland was replaced by an adrenocortical adenoma, so that only

a thin rim of normal adrenal cortex remained. The adenoma was composed of cords of fairly uniform rounded to polyhedral tumor cells which showed some variation from area to area. These cords were folded in some places. Foci of hemorrhage and necrosis were common. No mitotic figures were seen. In one area, pinkish-staining large bizarre cells with large blue-staining nuclei were noted. These cells showed considerable pleomorphism.

The small adenoma in the right adrenal gland was composed of pink-staining bizarre cells with marked nuclear variation in size and shape. They resembled cells of the fetal cortex. The capsule was intact in both adenomas. Fat stains revealed only a few small granules of fat in the tumor cells. Dichromate-fixed adenoma tissue revealed no chromaffin material.

Sections of the pons showed central hemorrhage, recent and massive. The smaller cerebral vessels showed a hyaline type of arteriosclerosis. Similar hyaline sclerotic changes were seen in small arteries throughout other organs.

The pituitary gland showed Crooke's hyaline changes in the basophiles with Mallory's aniline blue stain.[2]

COMMENT

Three features of this case merit comment: the early age of onset, the bilateral adrenocortical adenomas, and the early death from pontine hemorrhage.

The youngest patient with Cushing's syndrome whose case we could locate in the literature was that in the case recorded by Lightwood.[7] His patient was a boy whose symptoms began with enlargement of the cheeks and chin at the age of 11 weeks. When the infant was examined at 18 weeks, the cheeks were florid and there were hard deposits of fat around the cheeks, shoulders, and scapulae. There was a slight amount of abnormal hairiness on the forehead, the skin was dry and scaly in places, and the genitalia were normal. The legs were somewhat wasted. The child did poorly and died at the age of 4½ months. Autopsy revealed an adrenal "adenoma" about the size of the left kidney. In addition, there was marked hypertrophy of the left ventricle.

Another case of Cushing's syndrome with a very early onset of symptoms was reported by Marks and his associates.[8] Their patient was a girl showing monstrous obesity rather generally distributed. Her symptoms began at the age of 3 months with a ravenous appetite and rapid weight gain. When examined at the age of 10½ months, she was excessively obese, with enormous fat pads of the cheeks, chin, and shoulders. However, there were also large collections of fat in the mammary and abdominal regions and on the extremities, not in accord with the usual "buffalo" distribution. The skin was remarkably red, especially on the cheeks. On the forehead, cheeks, back, and pubic region there was an abnormal amount of brown hair. The genitalia were normal. The blood pressure varied from 200/100 to 245/145. The child died at one year of age, and necropsy revealed a 3 cm. adenoma of the right adrenal gland.

Our case, too, showed a rather general distribution of fat in addition to its presence in the usual "buffalo" and "moonface" locations.

According to the available medical literature, bilateral adrenocortical tumors or hyperplasia are rare in Cushing's syndrome. Indeed, atrophy of the opposite adrenal gland is the rule. In 1941, Weinberg reviewed 34 cases of neoplasm of the adrenal cortex in which both glands were examined at autopsy.[10] In 21 cases, the contralateral adrenal gland was atrophic; in 2 cases it was absent altogether. This becomes an important consideration when surgical removal of the tumor-bearing adrenal gland is planned. Removal of the hyperfunctioning adrenal tumor is generally accompanied by postoperative shock. Rapaport and his associates report the operative mortality for Cushing's syndrome associated with adrenal tumors as 56%.[9] The patients who survive are usually those that have been tided over the crisis period by adequate substitution therapy with adrenal cortex extracts. However, approximately one-half of those who survive the immediate postoperative period later develop recurrences or metastases. Goldstein reported a case of Cushing's syndrome in an 11-month-old infant who recovered after surgical removal of an encapsulated carcinoma of the adrenal cortex.[3] This

child was treated before and after operation with saline and adrenal cortex extracts. She appeared normal when last observed, one year after operation.

Goldstein recommended early operation to forestall death from tumor metastases, acute cerebrovascular and cardiovascular accidents, intercurrent infections, or inanition. Our patient presented two tumors; the smaller one would undoubtedly have been overlooked at operation and relapse would probably have occurred, even if the larger tumor had been successfully removed. The only other case of Cushing's syndrome with bilateral adrenal involvement that we could locate was reported by Chute and his associates.[1] Their case was that of an 8-year-old girl with nodular hyperplasia. She died two days after surgical removal of one adrenal gland.

Many authors have made general references to cerebral vascular accidents occurring in Cushing's syndrome, but specific instances of massive cerebral hemorrhage are apparently unusual. Certainly hypertension is the rule. Gross stated, "There may be other phenomena secondary to such hypertension, such as . . . headache or cerebral vascular accident."[4] He reported one case of Cushing's syndrome in a 10-year-old girl with a blood pressure of 148/120, which rose to 230 systolic. Terminally the patient developed convulsions. At autopsy, the brain showed petechiae, the heart was enlarged, and there was a carcinoma of the adrenal cortex. In our case, there was marked left ventricular hypertrophy and a large pontine hemorrhage, which was the immediate cause of death.

Microscopic sections of many organs revealed a hyaline degenerative arteriosclerosis in the smaller arteries. Such changes have been pointed out in other cases. These hyaline changes in the arteries of the brain may have predisposed to the terminal massive pontine hemorrhage.

SUMMARY

A case of Cushing's syndrome in a 12-week-old infant is reported; the patient is believed to be the youngest on record. At autopsy, bilateral cortical adenomas were found. The terminal episode was a massive pontine hemorrhage associated with hyaline arteriosclerosis and cardiac hypertrophy. The unusual features of the case are discussed.

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Progress in Pediatrics

PARTIAL THORACIC STOMACH AND ESOPHAGEAL HIATUS HERNIA IN INFANCY AND CHILDHOOD

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INTRODUCTION

The recent recognition of the syndrome of partial thoracic stomach in infancy has provided a diagnosis for a hitherto puzzling group of cases with vomiting as a leading symptom. As a result indefinite diagnoses such as "marasmus" or "dystrophy" are less frequent. This syndrome is associated with partial dislocation of the stomach within the thorax through the esophageal hiatus, the diaphragmatic leaves being intact.

It is the purpose of this paper to review present knowledge of the subject with particular reference to the younger age groups and to indicate rational management based on a consideration of the pathogenesis and prognosis. In this task the author has been aided by practical experience at the Hospital for Sick Children, Great Ormond Street, where over 100 cases have been followed for some years (Waterston, 1954). Discussion will be illustrated by reference to a small series of 18 cases personally examined by the author during the last 18 months at the Hospital for Sick Children, Toronto.

Much of the current confusion regarding pathogenesis and consequently rational treatment has arisen because of inadequate correlation of the observations of the numerous specialists whose common interest is within or around the esophagus and who frequently see a partial picture.

The modern tendency to regional specialization has resulted in many local diagnostic and therapeutic functions being vested in one clinician. Allison (1951) has correlated clinical, endoscopic, radiological, and operative findings to delineate precise syndromes and their management. Of these syndromes, by far the most important numerically is esophageal hiatus herniation with complicating reflux esophagitis.

This and related conditions are important in infancy and childhood and differ in some respects from the problems as seen in adults. However, only two relatively large series of cases in this age group have been published to date (Carré, I. J., Astley, R., and Smellie, J. M., 1952; Waterston, D. J., 1954). This contrasts with the numerous reports in adults.

There are a number of conditions where a portion of the stomach is above the diaphragm which superficially resemble each other but in which the pathogenesis is quite different. Controversy has centered around the question of whether there is developmental shortness of the esophagus, often with a congenital stricture (Clerf and Manges, 1934), or whether the position of the stomach is due primarily to herniation through the esophageal hiatus with secondary fibrotic shortening and stricture formation from reflux esophagitis (Moersch, 1938). It is now becoming clear that both views may be correct, though stricture formation is almost invariably secondary to reflux esophagitis irrespective of the primary condition.

SECTION I—THE DEVELOPMENTALLY SHORT ESOPHAGUS

There is a period between the 30th and 39th days (4-12 mm. embryo) of fetal development during which great elongation of the thoracic esophagus takes place in concert with the general caudal migration of the

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septum transversum and thoracic structures. During this time the esophageal lumen is temporarily attenuated (Hamilton, Boyd, and Mossman, 1952, pp. 221-222). Developmental faults at this stage might result in shortness of the esophagus and possibly stricture formation. The latter may be represented by the isolated membranous webs that have been reported, but, as Barrett (1950, 1954) has shown, if the literature is critically examined and strict criteria applied, undoubted examples of purely developmental shortness are rare.

Barrett (1950) quoted the fatal case of a boy of 13 years whose specimen was shown to him by Professor Barnard. This specimen had two small islets of ectopic gastric mucosa at the upper end of the gullet. Below these the esophageal mucosa stopped short. From the level of the arch of the aorta the mucosa was gastric and showed a large chronic ulcer which had perforated into a pulmonary vein. The original lesion was clearly a congenital short esophagus, and there was no suggestion of a diffuse esophageal fibrotic shortening or stricture. A similar case in a child is reported in his second paper (Barrett, 1954).

The present series of 18 cases contains one example of undoubted developmental shortness.

Report of Case

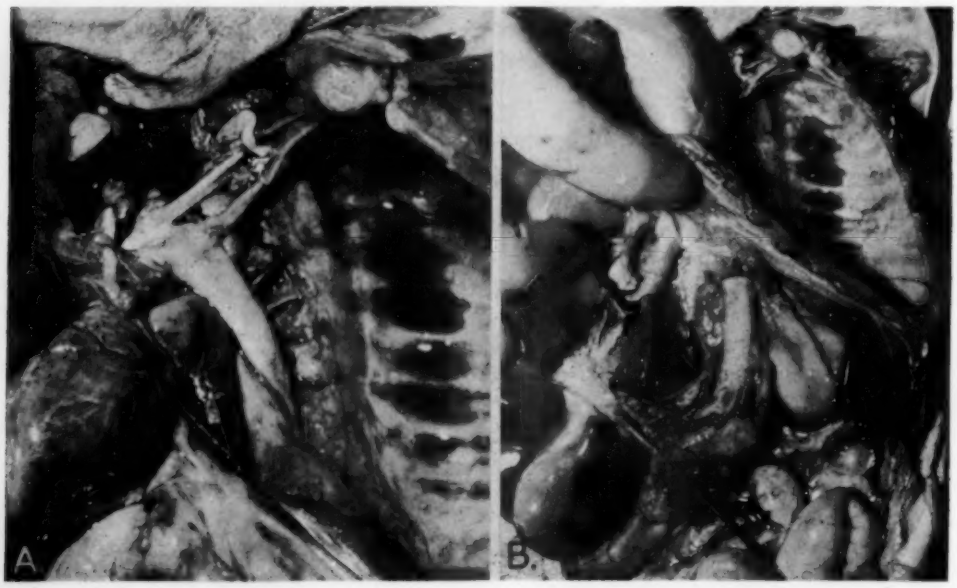
Case G. B.—This girl died at 6 weeks of age with multiple congenital anomalies including a nuchal meningomyelocele. There had been persistent vomiting since birth, and barium swallow had shown a malformed stomach with a supradiaphragmatic pouch. At necropsy the gastroesophageal junction could not be pulled down lower than 4 cm. above the upper margin of the hiatus even when dissected free from all surrounding structures below the arch of the aorta (Fig. 1). There was no evidence macroscopically or microscopically of esophagitis or periesophagitis, and there was no narrowing of the esophagus or esophagogastric junction. About one-third of the stomach was in the chest and assumed a tented shape, being clearly differentiated morphologically from the tubular esophagus above. There was no peritoneal hernial sac.

Other congenital anomalies included malformation of the stomach, abnormally short duodenum, small pancreas, absence of the greater omentum, aberrant renal vessels, and the nuchal meningomyelocele which had been repaired surgically.

Death was ultimately due to aspiration pneumonitis.

The absence of esophagitis or inflammatory fibrotic shortening suggests that there had been a true failure in longitudinal development.

Fig. 1.—*A*, tent-shaped portion of stomach is seen above the diaphragm. *B*, the deformity of the stomach below the diaphragm.



This leads to the question whether all cases of partial thoracic stomach cannot be explained on the basis of a developmentally short esophagus. There is overwhelming evidence against this. The most compelling is that surgeons who have operated on these cases find that, in nearly all, it is possible to replace the stomach below the diaphragm without strain. In all 62 of the cases operated on at Great Ormond Street replacement was possible. At operation the vagus nerves appeared slack and only took up their normal tightness when the stomach had been replaced in the abdomen. In Belsey's series of 94 cases (1952) there was not a single instance of shortening in the absence of active or healed esophagitis. Allison found only one example of true shortening in 204 cases of all ages.

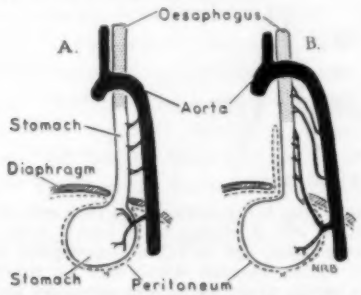


Fig. 2.—Blood supply of the short esophagus and of sliding hiatus hernia. *A*, developmentally short esophagus. The mediastinal tube lined by gastric mucosa is supplied by segmental branches from the aorta. *B*, true hiatus hernia. The herniated intrathoracic portion of the stomach is supplied by branches of the left gastric artery. Reproduced with permission from Barrett, N. R.: *Brit. J. Surg.* 42: 231-243 (Nov.) 1954.

Harrington (1955) reported a higher incidence of 5% congenital shortness in 489 cases of all ages. Sweet (1952) found congenital shortness in 4.5% of 111 cases.

Barrett (1954) stated that the blood supply of the stomach and esophagus is an additional guide in defining the developmentally short esophagus from hiatus herniation. Figure 2*A*, from his 1954 paper, demonstrates that where the esophagus is developmentally short the whole of the intrathoracic tube, whether lined by esophageal or by gastric mucosa, is supplied by segmental branches from the aorta. In the case of primary hiatus herniation the supradiaphragmatic portion of the stomach is supplied by branches of the left gastric artery (Fig. 2*B*).

There are two anatomical varieties of the developmentally short esophagus. In one the external morphology of the intrathoracic tract is tubular but gastric mucosa extends up the tube in an unbroken sheet to a variable, but usually high level (Fig. 3*F*). In the other (Fig. 3*G*) the external morphology of the intrathoracic tube changes unmistakably to the usual tented form of a supradiaphragmatic stomach pouch, as demonstrated by Case G. B. (Fig. 1).

There is therefore evidence that true esophageal developmental shortness can occur but is a rare anomaly. Such cases do not usually present with reflux esophagitis and consequent stricture formation above the esophagogastric junction but with one of the complications of a true peptic ulcer, namely, perforation, massive hemorrhage, or carcinoma in adults. One exception to this rule has been reported by Bosher and Taylor (1951), whose case of gastric-lined esophagus had a stricture due to reflux esophagitis above the aortic arch.

SECTION II—ESOPHAGEAL HIATUS HERNIA: TYPES

By comparison, cases of partial thoracic stomach where the shortening of the esophagus is apparent only or due to muscular or fibrous retraction in association with esophagitis are much commoner.

At this point it is necessary to define the anatomical types of hiatus hernia. Figure 3*A-E* illustrates these diagrammatically. The commonest is the sliding hiatal hernia (Fig. 3*A-C*), which usually has a partial hernial sac of peritoneum on the left side (Fig. 3*A*). Then there is the rolling paraesophageal hiatus hernia, where the fundus or anterior surface of the stomach rolls around the fixed cardiopyloric axis into a persistant pneumatoenteric recess (Hamilton, Boyd, and Mossman, 1952 [pp. 221-222], Barrett, 1954, Morris, 1954), probably passing through the margin of the crus (Fig. 3*D*). The fragment of crus between the hernia and the hiatus may disappear entirely, so that the hernia passes through the hiatus itself into the lower dorsal mediastinum toward the right. This type is

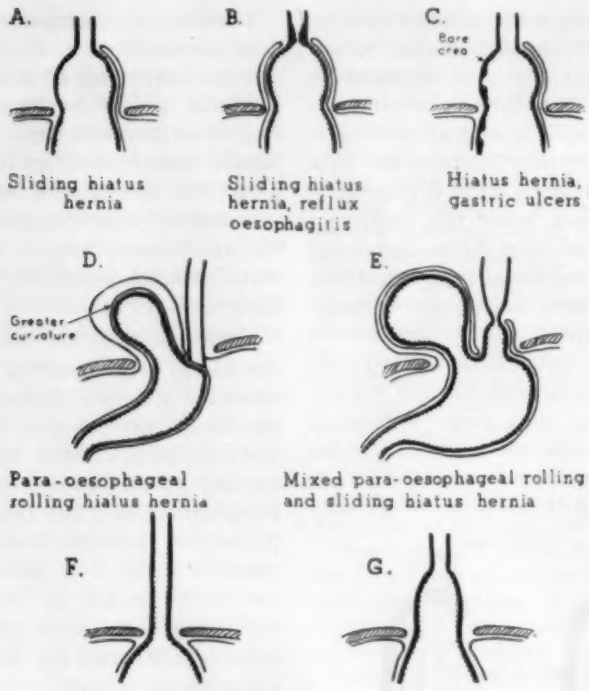


Fig. 3.—Varieties of partial thoracic stomach. *A*, the sliding hiatus hernia with bare area of stomach above the diaphragm on the right and a sac on the left. *B*, sliding hiatal hernia with a complete sac. Inflammatory thickening of the lower esophagus, due to reflux esophagitis, is shown. *C*, sliding hiatus hernia with peptic ulceration in the stomach which may be either above or below the diaphragm. *D*, paraesophageal hiatus hernia where the greater curvature and fundus of the stomach have rolled around the fixed cardiopyloric axis into a preexisting sac passing either through the fibers of the right crus or through the hiatus itself. The cardia is below the diaphragm and is competent. *E*, mixed paraesophageal and sliding hiatus hernia. The cardia is above the diaphragm and is usually incompetent, exposing the patient to the dangers of reflux esophagitis, F, developmental short esophagus with failure of morphological differentiation between esophagus and stomach. There is a tubular structure above the diaphragm lined internally with gastric mucous membrane but externally resembling the esophagus. *G*, developmentally short esophagus with morphological differentiation between stomach and esophagus above the diaphragm. The esophagus is primarily short, and the cardia cannot be replaced below the diaphragm as in the case of a sliding hernia.

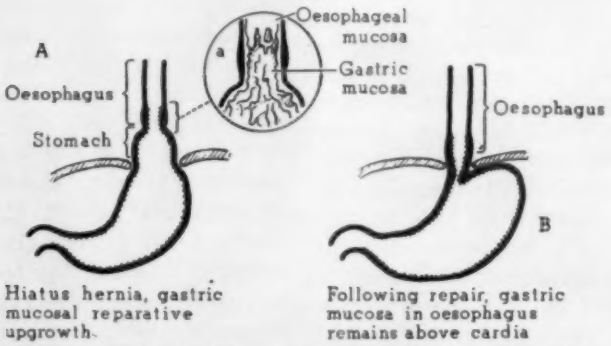


Fig. 4.—To illustrate Allison's (1953) suggestion that gastric mucosa could invade the lower esophagus following reflux esophagitis. Histologically esophageal glands were often found deep to an area of gastric mucosa above the cardia in Allison's specimens.

rare in childhood. Husfeldt (1953) reported its presence in only 2 out of 56 cases of hiatus hernia. Since the cardia is in its normal position below the diagram, it remains competent and reflux esophagitis does not occur, in contradistinction to the situation with the sliding hernia. The third variety is the mixed, sliding and paraesophageal rolling hernia, where esophagitis is a definite hazard (Fig. 3*E*). This classification has been elaborated from that by Åkerlund (1926).

There is one further possible explanation for the presence of gastric mucosa in the lower esophagus. Following erosion by reflux, repair may be upward extension of gastric mucosa (Allison 1953) (Fig. 4). There is histological support for this conception in the finding of esophageal mucus glands deep to gastric mucosa in some of Allison's cases. This group may account for some of the occasional poor results of operation, since gastric secretory mucosa remains above the cardia after apparent satisfactory repair. It may also be the explanation of the cases described by Thomas, Rappaport, and Keogh (1954) of obstruction to the lower esophagus by diseased ectopic gastric mucosa.

SECTION III—ESOPHAGEAL HIATUS HERNIA: PATHOGENESIS

It is now necessary to seek the answer to two related questions. Firstly, what are the mechanisms maintaining the cardia below the diaphragm, and secondly, on what does the competence of the cardia depend?

Maintenance of the Cardia Below the Diaphragm

In normal persons the left gastric artery and its mesentery hold the cardia in its normal position (Barrett, 1952, 1954). If these structures are lax, the cardia is permitted to ride up into the thorax, and the intrathoracic loculus can be seen at thoracotomy to be supplied by branches of the left gastric artery (Fig. 2*B*). The phrenoesophageal condensations of fibroelastic tissue are believed by some to be important tethers. Surgeons of wide experience differ on the efficiency of these condensations, and this renders their importance suspect.

The influence of size and shape of the hiatus must be considered. Collis, Kelly, and Wiley (1954) have recently produced evi-

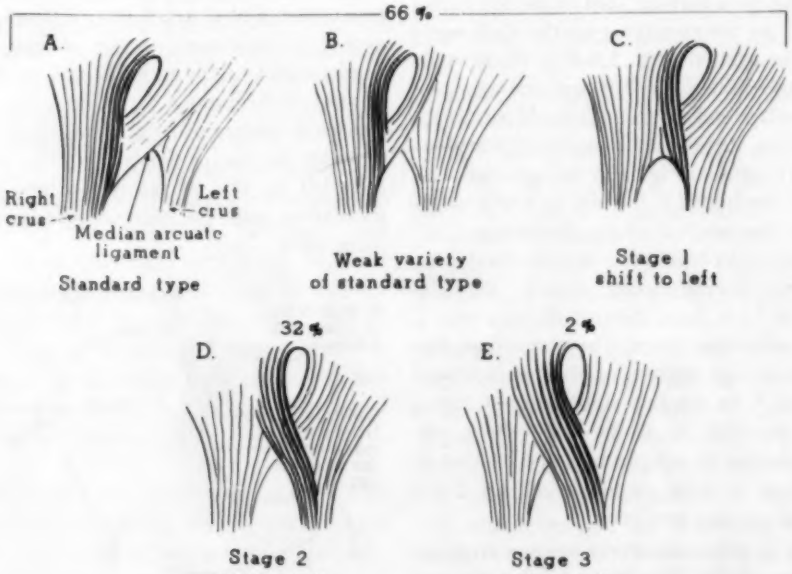


Fig. 5.—The anatomy of the crura of the diaphragm, based on the work of Collis, Kelly, and Wiley (1954).

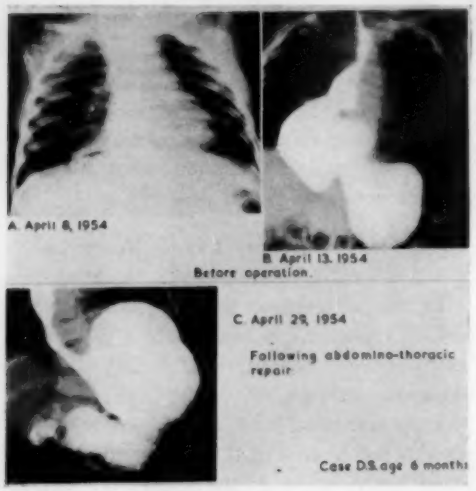


Fig. 6.—Case D. S. Mixed sliding and paraesophageal hernia in a child of 6 months, with a hiatus admitting three fingers at operation.

dence of variation in the degree of development and arrangement of the fibers of the right crus of the diaphragm, which usually form the hiatus. Their paper is based on dissections of 64 diaphragms. These workers showed that there is a varying degree of overlapping of muscle fibers making up the hiatus, depending on a varying shift to the left in the origin of the fibers making up the right margin of the hiatus (Fig. 5*A-E*). Those with no or little shift to the left and consequently little overlap tend to have a weak hiatus (Fig. 5*B*). Three stages of shift to the left are described, Stage 3 (Fig. 5*E*) being where the whole of the hiatus is formed by fibers originating in the left crus of the diaphragm. Certain reinforcing transverse muscle bands, the transverse intertendinous muscle, and the muscle of Low (not illustrated) also play a part in individual cases. The percentage distribution of the degrees of shift is indicated in Figure 5. In a series of 18 cases of hiatus hernia reported by Collis and others, the hiatal muscles at operation could be classed as medium or weak, while in all but 2 the degree of overlap was poor.

There is still controversy among surgeons about the relative importance of the size and anatomy of the hiatus. Barrett regards it as of secondary importance and stated that he found it hard to define a normal hiatal size (1954). It is difficult to deny some role to an abnormally large hiatus in a case such as the following.

Report of Case

Case D. S.—This infant was brought to hospital because of a mild febrile convulsion. A radiograph of the chest was taken and an abnormal shadow noted behind the right heart (Fig. 6*A*). This was subsequently shown by barium examination to be an intrathoracic loculus of stomach as part of a mixed paraesophageal and sliding hiatal hernia (Fig. 6*B*). Inquiry revealed that the baby had vomited from birth and that the mother had noted a splashing sound in the lower chest on swallowing. She had found by experience that vomiting was diminished by maintaining the infant in an upright position. The x-ray also revealed hemivertebrae at the 10th and 11th dorsal levels, and at operation the hiatus admitted three fingers. This is certainly abnormally large for a child of 7 months.

Another factor may be involved in regard to the hiatal orifice. The crural fibers encircle the lower end of the esophagus rather as the puborectalis muscle encircles the rectum. Allison regarded this encircling action in both muscles as important in closing off the respective tubes. This is true, but the sling has another and more important function. The hiatal muscle sling fits into the incisural groove between stomach and esophagus. This groove is dependent on the oblique muscle condensation at the incisura and on the distention of the fundus by fluid or gas. If the groove is maintained the hiatal sling will be a tether for the cardia in addition to those afforded by the left gastric artery and its mesentery and the phrenoesophageal ligament (Fig. 7).

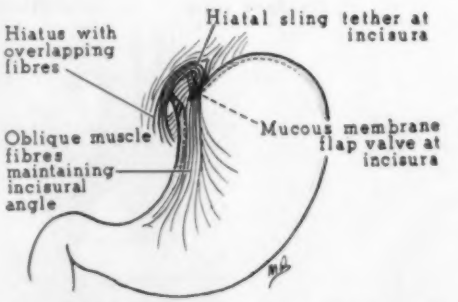

Hiatal sling tether at incisura
Hiatus with overlapping fibres
Oblique muscle fibres maintaining incisural angle
Mucous membrane flap valve at incisura

Fig. 7.—The anatomy of the cardia, with some of the extrinsic and intrinsic mechanisms of competence.

These factors making for stability of the cardia are peculiar to the individual and dependent on developmental, anatomical variation. It is conceivable that those individuals born with a high degree of mobility of the cardia will present with hiatus herniation neonatally. Data from this and other papers suggest that this is a not inconsiderable group. Lower degrees of motility may only result in herniation if some special strain is placed on the orifice. In infants there are several reports of the association of congenital pyloric stenosis with hiatus hernia (Pilcher, 1951; Waterston, 1954); it is tempting to postulate that the distention of the stomach and frequent violent vomiting, by raising intra-abdominal pressure, can cause herniation of an inherently mobile cardia. In adults hiatus herniation is commonest over the age of 50 years, where obesity raising intra-abdominal pressure, lack of muscular tone, and diminution in elastic tissue have been suggested as factors. Similar considerations in regard to raised intra-abdominal pressure may explain the frequency of hiatus herniation during pregnancy (Rigler and Eneboe, 1935; Allison, 1943; Rennie, Land, and Park, 1949; Nicholson, 1952).

Other intra-abdominal disease, such as cholecystitis, by reflex vagal stimulation may cause longitudinal contraction of the esophagus, thus pulling the stomach up (Smithers, 1950). This theory does not account for the many cases where no other disease is present, especially in childhood, and the balance of evidence is against it. Gilbert, Dey, and Rall (1946) gave etiological importance to emotional and reflex factors and subscribed to the vagal-stimulation theory. However, the ill humor of many infants with hiatus hernia is more likely to be due to the pain of esophagitis than to be the cause of vagal stimulatory esophageal retraction.

The Mechanism of Competence at the Cardia

Dornhorst, Kent Harrison, and Pierce (1954) have shown by simultaneous radiology with barium swallows and capacitance electromanometric pressure readings in the esophagus and stomach of normal subjects that the functional cardiac valve extends over about 5 mm. at the esophagogastric junction and offers a resistance to forward flow into the stomach of approximately 4 mm. of mercury. The time required for the cardia to yield to a bolus (0.5 seconds) suggested more a valvular than a sphincteric mechanism to the authors. During a moderately deep inspiration there is a pressure difference of 15 mm. of mercury between stomach and esophagus favoring reflux. During strong inspiration against a closed glottis, this pressure differential was shown to rise to as much as 80 mm. of mercury (Fig. 8). In both cases there was no tendency for the pressures to equalize, indicating complete competence of the cardia. From observations on the human stomach at operation these authors believed that extrinsic mechanisms had little to do with competence of the cardia. They postulated that the muscularis mucosa pulled the lax mucosa at the cardia into some flap or funnel valvular form. In two cases at operation, manipulation of the cardia with the

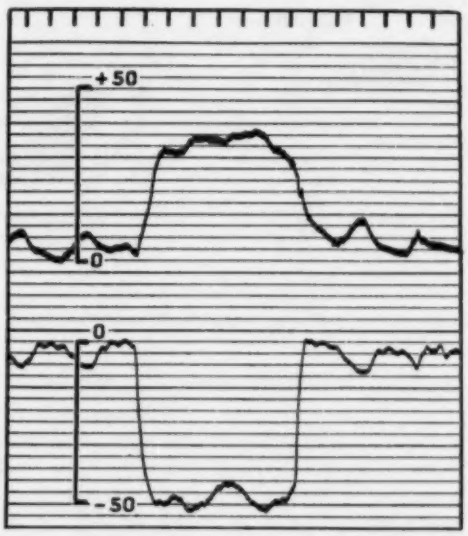


Fig. 8.—Pressures in the stomach (upper trace) and esophagus (lower trace) of a normal individual during strong inspiration against a closed glottis (Müller's procedure). Note that there is no tendency to equalization of pressures indicating complete cardial competence. Reproduced with permission from Dornhorst, A. C.; Harrison, K., and Pierce, J. W.: *Lancet* **1**:695-698 (April 3) 1954.

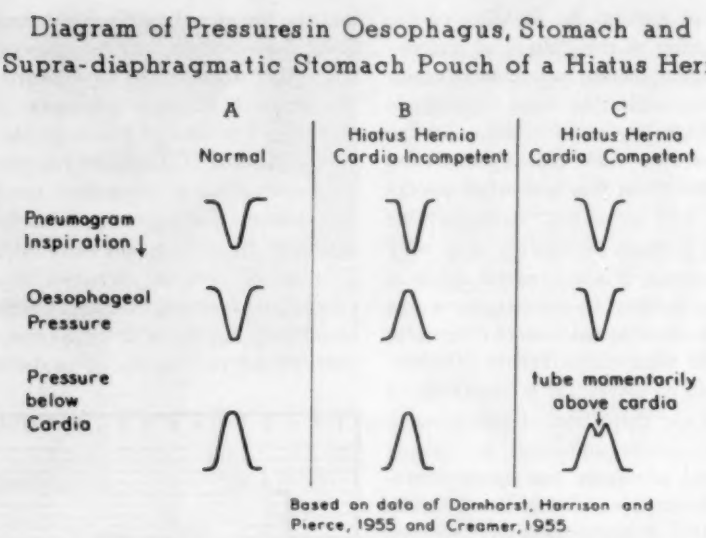


Fig. 9.—*A*, the inverse relationship of pressure in the esophagus and stomach is shown in a normal subject. *B*, the congruence of pressures in the esophagus and stomach is shown in the case of a patient with a hiatus hernia and an incompetent cardia. *C*, the pressures in another case of hiatus hernia show the normal inverse relationship indicating cardial competence. A momentary fall in pressure is registered where the pressure recording tube slips above the cardia.

fundus making approximately a right angle with the esophagus produced gastroesophageal incompetence. They discounted the influence of the angle of entry of the esophagus.

This electromanometric work has recently been extended by Creamer (1955). He has shown that the occurrence of reflux initiates a positive pressure wave in the esophagus and that in the presence of esophagitis heartburn followed within 30 seconds. He further showed that in some patients with hiatus hernia, instead of the normal inverse relationships (Fig. 9*A*), pressure changes in the herniated stomach and in the esophagus were closely comparable, indicating persistent incompetence at the cardia (Fig. 9*B*). In the majority of examples of hiatus hernia the pressure changes across the cardia showed that incompetence was not constant (Fig. 9*C*). This supports Aylwin's (1953) observation that many cases of hiatus hernia do not have reflux and so do not develop esophagitis. Some changes in bodily position, even in normal individuals, were associated with reflux, though such changes did not cause any important rise in the pressure differential across the cardia. Consequently Creamer considered that, when bodily position was varied, alteration in the anatomical configuration of the cardia and its postulated mucosal flap valve permitted reflux. Reflux was most likely to occur while lying supine or when bending forward.

Support for this idea of an intrinsic mucosal valve as the primary agent of competence of the cardia comes from the observation that, if a thoracoscope is passed into the stomach at operation, it is extremely difficult, if not impossible, to discern the cardiac orifice, owing to pouting of the mucosa (Barrett, 1954). Further support comes indirectly from O'Mullane's (1954) observation that total somatic and therefore phrenic paralysis by muscle relaxants during anesthesia, even when associated with the Trendelenburg position, did not result in gastric reflux into the esophagus. It is unlikely, therefore, that the "diaphragmatic pinch-cock" is of major importance in securing competence.

It is common knowledge that there is no anatomical cardial sphincter. The presence of a functional sphincter has hitherto been inferred from the radiological observation that a column of barium frequently remains ap-

parently held up in the esophagus for some seconds before being swept on into the stomach by a peristaltic wave. Dornhorst and others (1954) suggested that this momentary hold-up could equally well be due to the normal pressure differential across the cardia before it is annulled by a peristaltic wave. It is difficult to invoke an important sphincter mechanism which does not exist anatomically, and there are good experimental grounds for accepting Dornhorst's and his associates' explanation of the radiological appearance.

It has been shown experimentally with the isolated stomach and esophagus that the more acute the angle of entry of the esophagus into the stomach, the higher the pressure needed

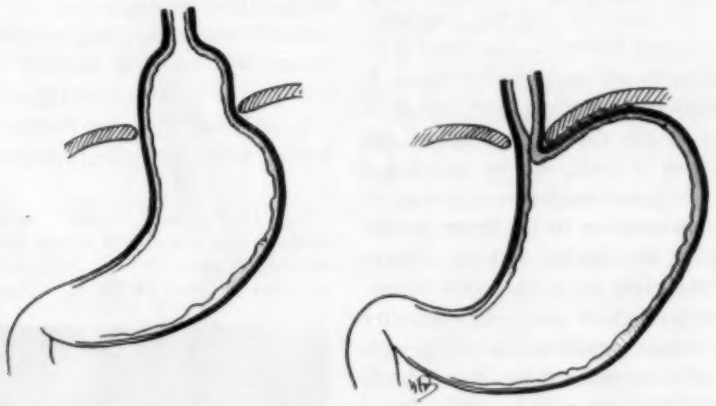


Fig. 10.—Illustrating the effect of operative reduction of a hiatus hernia in restoring the normal anatomy of the cardia.

within the stomach to produce reflux (Barrett, 1952, Collis, Kelly, and Wiley, 1954). Anatomically the intrinsic oblique muscle fibers of the stomach form the apex of the incisural angle (Fig. 7). It is in maintaining this incisural angle that the extrinsic mechanisms reinforce the intrinsic. The crural fibers of the hiatus loop over the incisura and help to maintain the angle and close the esophageal tube. Furthermore, in inspiration, when the pressure differential across the cardia is greatest in favor of reflux, the crural fibers contract in unison with the rest of the diaphragm, pulling down the incisura and so preventing a widening of the angle. The importance of this angle in securing competence is shown by the success of operations designed for its reconstitution.

The mucosal valve and the incisural angular theories of closure of the cardia are complementary in that restoration of the angle in a given case of hiatus hernia would enable a presumed mucosal flap valve to function (Fig. 10).

SECTION IV—THE SYNDROME OF REFLUX ESOPHAGITIS

History

In 1919 Pringle and Teacher described 15 cases of severe fatal illness characterized by vomiting where severe antemortem digestion of the lower esophagus had occurred. The significance of these observations was not generally appreciated for some years. In 1929 Chevalier Jackson, in a paper on ulceration of the esophagus, ascribed the lesions primarily to septic foci usually in the tonsils though he did not exclude the possibility that gastric reflux tended to perpetuate ulceration. Also in 1929, Friedenwald, Feldman, and Zinn reported 13 cases of ulceration in the lower esophagus. While recognizing the importance of gastroesophageal reflux, these authors felt that the esophageal ulceration was etiologically similar to ulceration elsewhere in the upper alimentary tract. They did not remark on the presence of hiatus herniae, though some of their radiographs

are suggestive. From 1938 onward a number of authors suggested the primary etiological importance of gastric reflux in the causation of ulceration of the lower esophagus (Moersch, 1938; Briggs, Dick, and Hurst, 1939; Feldman, 1939; Allison, 1943; Johnstone, 1943). In 1950, Ferguson, Sanchez-Palomera, Sako, Clatworthy, Toon, and Wangensteen showed experimentally the dramatically deleterious effect of acid peptic juice perfused through the esophagi of living animals. The experiments often culminated in perforation within one hour. Allison and his co-workers (1943, 1946, 1948, 1951), Barrett (1950, 1952, 1954), and Belsey (1952, 1953, 1954), in a series of papers during the last 12 years, have been largely responsible for pointing out the frequency with which hiatus hernia is associated with reflux esophagitis and stricture formation. It is now generally recognized that failure of competence at the cardia is primary and ulceration and fibrosis in the esophagus secondary. To avoid confusion it is well to designate inflammation in the lower esophagus as reflux esophagitis with or without ulceration reserving the term peptic ulceration for that type which occurs on absorptive alimentary mucus membrane only. The syndrome of reflux esophagitis has also recently received further attention in the United States. Schmidt (1954) and Carver and Sealy (1954) reported 170 and 130 cases, respectively. The vast majority in both series were associated with hiatus hernia.

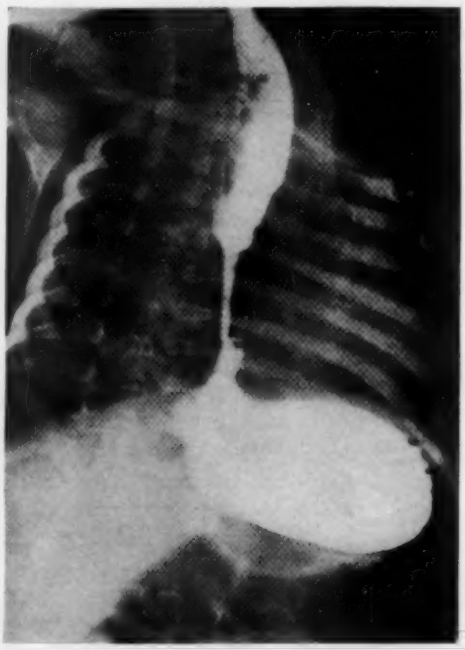
Pathology

Hiatus herniation is common, but not all cases develop reflux esophagitis or stricture. Aylwin (1953) carried out some experimental work in an attempt to reconcile these facts. He reasoned that daytime reflux was limited by upright posture in adults and that such reflux as occurred was rapidly neutralized by a protective alkaline salivary and esophageal secretion which could amount to many times the normal adult 1.5 liters daily due to irritative vagal reflex stimulation of flow.

At night the horizontal posture and incompetent cardia, in a proportion of cases, permit reflux which is not neutralized by salivary or esophageal secretion. By collecting this night reflux with continuous suction on an indwelling esophageal tube he showed that the volume, reaction, and pepsin concentration could be correlated with the presence and degree of esophagitis. If a sufficient volume of pepsin-containing juice at the right pH was recovered, the case invariably presented evidence of esophagitis. These experiments were carried out on adults, but there is no reason to believe any essential difference would be found in infancy and childhood. In infants who spend most of their life horizontally there is not the adult distinction between night and day in terms of posture. Thus reflux may be more sustained, though this could be partially offset by an increased flow of neutralizing juices.

In addition to the mechanical factors permitting reflux and the physiological factors

Fig. 11.—Barium swallow outlining a long stricture in a 6-week-old infant. Reproduced with permission from Belsey, R.: *Ann. Roy. Col. Surgeons England* **14**:302-322 (May) 1954.



controlling neutralization of peptic activity. Aylwin produced evidence that variations in the relative numbers of pepsin-producing and oxyntic cells in the supradiaphragmatic pouch affect the degree of esophagitis.

Alkaline digestive juices from the duodenum may reflux, and this might be the cause of esophagitis, especially where partial gastrectomy and esophagogastrostomy has been performed.

Esophagitis may quickly produce severe stricture formation. Figure 11, from Belsey's 1954 paper, shows a long stricture in a 6-week-old baby. Others have also emphasized the rapidity with which a stricture can form in infants (Waterston, 1954; Hodgson, 1954). The stricture may be either localized or may involve a considerable length of the lower esophagus. Figure 12 illustrates these

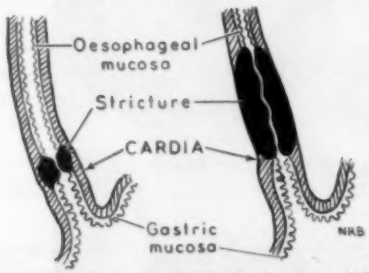


Fig. 12.—Diagram to illustrate the two different types of stricture which occur as a complication of reflux esophagitis. That on the left is the common linear variety. That on the right represents "ascending esophageal fibrosis." Reproduced with permission from Barrett, N. R.: *Brit. J. Surg.* 42:231-243 (Nov.) 1954.

types. A photograph of a resected longitudinal stricture (Fig. 13, Mr. Belsey's case) shows the extreme degree of narrowing and extensive infiltrative fibrosis which may develop in a 5-year-old child.

These facts should point the need for careful control of all cases with symptoms suggestive of reflux esophagitis, including esophagoscopy.

SECTION V—ESOPHAGEAL HIATUS HERNIA: PROGNOSIS

Some idea of the mortality before a rational therapy based on an appreciation of the pathogenesis was practiced can be gained from some of the early literature.

Beatty (1928), in a paper entitled "Congenital Narrowing of the Œsophagus," summarized 50 cases from the literature and added 8 of his own, 3 of which were museum specimens. Thirty-five of these fifty-eight cases have sufficient detail for one to be reasonably sure that they were examples of hiatus herniation complicated by stricture formation. In all, symptoms dated from infancy, and in many, from birth. Nine of these thirty-five died. Seven died before the age of 4½ years. The average length of survival was 19 months. Three of these childhood deaths were due to virtually complete obstruction of the esophagus at the stricture. The fourth died of extreme emaciation, the fifth of wasting and bronchopneumonia, and the sixth of pneumonia following gastrostomy. The last case suffered a perforation of the esophagus by a catheter. Two women survived to the ages of 46 and 59 years, respectively. One died of dysphagia pneumonitis and the second of wasting. Necropsy in this case displayed esophageal ulceration, periesophagitis, and sinuses tracking into the lungs. The total mortality then in this group of 35 cases of presumed hiatus herniation was 9, or approximately 26%.

Sheldon and Ogilvie (1929) reported 12 cases of obstruction of the esophagus in children. In retrospect they were probably primarily due to hiatus herniation. Five of these twelve died. In one the cause of death was tuberculous meningitis. The esophagus was said to be normal at necropsy in spite of a radiological finding of obstruction of the level of the seventh thoracic vertebra two and one-half years previously. In one case there was no necropsy. Two others died with extreme wasting and marked stricture formation, while the last case died of bronchopneumonia after repeated bouginage. There was a thick fibrous stricture just above the diaphragm.

It is possible that an underlying hiatus hernia may be present in a number of infants dying from aspiration pneumonitis or acute aspiration of vomitus, since vomiting occurs independently of stricture formation, and a small hiatus hernia may not be detected at necropsy.

As the full picture of hiatus hernia in childhood has only recently been recognized, too

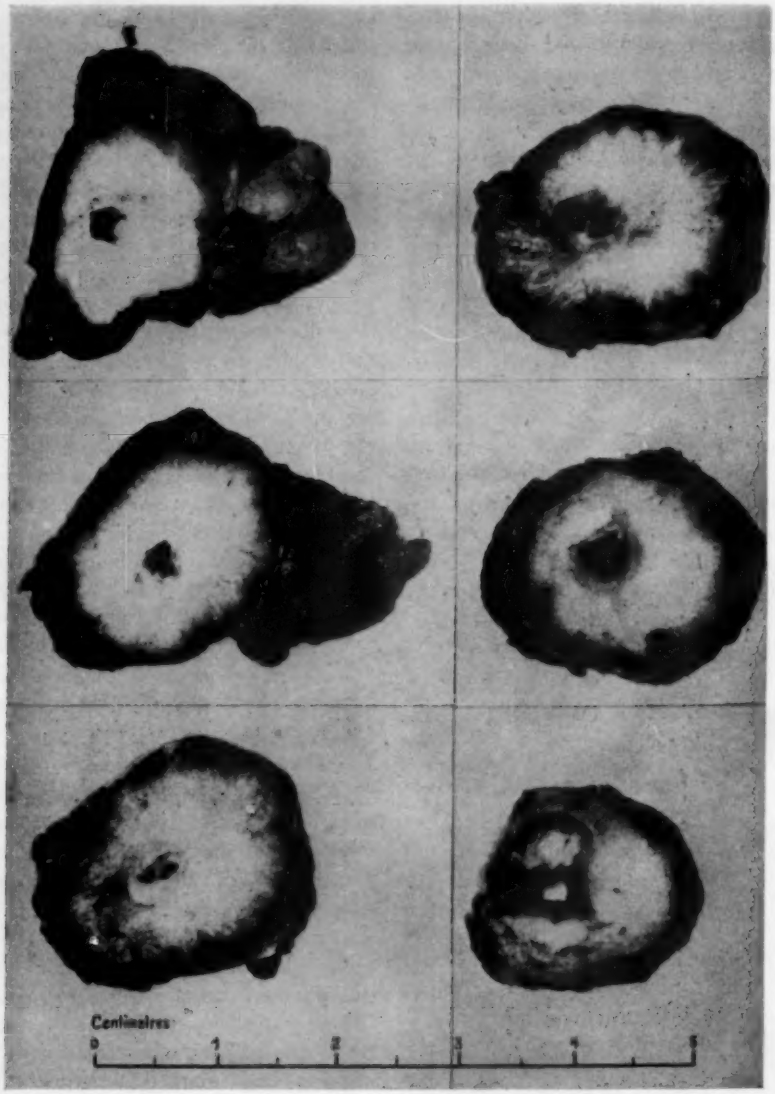


Fig. 13.—Sections taken at successive levels from a stricture removed from a 5-year-old child by Mr. Ronald Belsey. Reproduced with permission from Belsey, R., in "Modern Trends in Gastro-Enterology," edited by F. Avery Jones, London, Butterworth & Co., Ltd., 1952, p. 145.

short a period has elapsed for a satisfactory appraisal of the natural history. There is only one record of a prolonged follow-up in the literature. In 1931 Findlay and Brown Kelly reported nine cases of what was then called "Congenital Shortening of the Œsophagus and the Thoracic Stomach Resulting Therefrom." In 1953 Brown Kelly's son, H. D. Brown Kelly, was able to trace six of these nine cases. All required repeated esophagoscopic dilatations during childhood. Twenty-two years later none of these six cases was symptom-free, though all were in good condition and leading relatively normal lives. Five out of the six complained of dysphagia or retrosternal pain. Five still had a greater or less degree of regurgitation. Two needed special finely divided food and on

barium swallow showed a partial stricture in the esophagus. In a third case no mention was made of a stricture radiologically and no hernia could be detected. The case was not esophagoscoped. The patient complained of retrosternal pain and daily regurgitation in spite of the negative radiological findings.

One case has been followed in this hospital for 12 years.

Report of Case

Case T. Y.—This boy was first seen at the age of 9 months, in 1943. There had been vomiting since one month of age, with occasional small hematemeses. He was not seen again until he attended at 10 years of age, when esophagoscopy disclosed a stricture apparently in the midportion of the esophagus. This was dilated. After this he swallowed mercury bougies at home and progressed well. In recent months vomiting has become severer, and he returned to hospital at the age of 12 years 7 months, weighing only 56¼ lb. Repeat esophagoscopy now shows the stricture as before with ulceration which bled temporarily (Fig. 14). A 7×35 mm. esophagoscope was passed through the stricture without difficulty. The gastroesophageal junction was seen above the hiatus.

Fig. 14.—Case T. Y., age 12 7/12 years, showing stricture formation. The tubular structure below the stricture is the supradiaphragmatic pouch of stomach.

There are several series of cases in infancy and childhood with a shorter term follow-up reported from Copenhagen (Wamberg, 1947; Thomsen, 1949; Gertz, Regout, and Thomsen, 1951; Husfeldt, Thomsen, and Wamberg, 1951). Husfeldt (1953) has recently summarized the results of the Copenhagen group with conservative and operative (Appendix) treatment. He reported 25 conservatively treated cases under the age of 2 years when first seen. The exact length of follow-up is not clear. In two of the four deaths, the fatality was probably due to the hiatus hernia, since one died of "severe dyspepsia" and the second after jejunostomy for extreme emaciation.

Four patients had practically no symptoms, but barium swallows showed in three a long smooth stenosis of sufficient caliber to permit swallowing of carefully masticated food but which made regurgitation difficult. The fourth patient still had a hernia but no stenosis. In seven the hernia was no longer radiologically discernible. No useful information was available on the remaining nine patients.

Waterston (1954), in an interim report on the cases treated at Great Ormond Street, had 132 cases under observation. In 62 of these operative replacement and repair of the hiatus had been carried out because of the threat or occurrence of complications, chiefly esophagitis and stricture formation. The remainder were responding satisfactorily over a relatively short period to conservative treatment. Twenty cases, or one-third of those operated on, had strictures in infancy or childhood.

Belsey (1952) reported that operation was necessary in 13 out of 14 children in his series. This may have been a selected group, as he was writing from a thoracic surgical unit. His indications for operation were duodenal obstruction in two, hemorrhage and anemia in two, and severe esophageal obstruction in nine. In a later paper (Belsey, 1954) he reported 50 childhood cases, out of 250, below 10 years of age. Seventy-five per cent of these cases, when first seen, had esophagitis.

In rather less than half of Waterston's series in infancy and childhood there was either established or threatened stricture formation due to esophagitis.

Against this is to be set the experience of the group in Birmingham, in children, where less than 10% of the cases diagnosed in infancy were thought likely to develop an esophageal stricture (Smellie, 1954). It is presumed that this figure would apply to medically treated cases. From the same source Carré and others (1952) reported that only one case of esophageal stricture has been admitted to the Children's Hospital, Birmingham, yearly in the preceding 16 years. In contrast, in one year (1951) 18 cases of partial thoracic stomach were admitted. They suggested that about three-quarters of all cases run a benign course with symptomatic if not anatomical cure. Of the remaining quarter, the majority lose their symptoms around 4 years of age, but a few progress to stricture formation. Only one of their 112 cases developed a stricture under observation. Their follow-up is still in progress.

The Birmingham estimate of the number developing strictures (less than 10% of 112 cases) is a fair approximation to the numbers with stricture in the Great Ormond Street series (15% of 132 cases). It is in the relative assessment of the risk of esophagitis and stricture formation that the difference between the two groups lies.

The published incidence of esophagitis and stricture formation in 1177 cases of hiatus herniation at all ages has been summarized in Table 1. This shows the incidence of esophagitis to be 43% and of stricture 17.7%. Two series of cases of reflux esophagitis due predominantly to hiatus herniation but also including a number of other causes are shown separately. These two series have not been used in the calculations of incidence of stricture formation.

TABLE 1.—*Published Incidence of Stricture and Esophagitis in Cases of Partial Thoracic Stomach*

Author	No. Cases	Age Group	Esophagitis		Strictures	
			No.	Per Cent	No.	Per Cent
Allison (1951)	176	Mostly adult	73	41	63	37
Carré, Astley, and Smellie (1952)	112	Children	NK*	NK	NK	<10
Waterston (1954)	132	Children	42	32	20	15
Belsey (1954)	50	Children	37	75	20	40
Nicholson (1952)	42	Adults	19	45	6	14
Evans (1952)	176	Adults	NK	NK	26	14.7
Harrington (1955)	480	Adults	NK	NK	63	13†
Total	1,177	All ages	171/400	43	208	17.7
		Reflux Esophagitis				
Carver and Sealy (1954)	130‡	Av. age 51 years	130	100	83	65
Schmidt (1954)	170§	Adults	170	100	80	47

* NK indicates not known.
† This 13% includes some with malignant strictures in adults.
‡ Only 98 (76%) of these 130 cases of reflux esophagitis were associated with a hiatus hernia.
§ 158 (93%) of these 170 cases of reflux esophagitis had hiatus hernia.

It may be that the published figures give an unduly high estimate of the incidence of stricture compared with the incidence of hiatus hernia, since most series emanate from surgeons in largely adult clinics who would be more likely to see complicated cases.

This argument does not hold for the Birmingham series (Carré and others, 1952) or for Waterston's Great Ormond Street series (1954), both of which represent the full experience of cases of hiatus hernia in large children's hospitals. A pediatrician should be conscious of the possible remote effects in adult life of the conditions which he is called upon to diagnose and treat. In fact, he has a special responsibility to hand on his charges to the adult physician without a disability that

could have been prevented or eliminated by diagnosis and correct treatment in early life.

The frequency of stricture formation causing important symptoms suggests that a serious view should be taken of an esophagitis which does not yield quickly to conservative treatment. This view is strengthened by the several reports in the literature of serious stricture formation occurring within two to three months (Fig. 11), while the cases were under observation (Allison, 1951; Waterston, 1954; Hodgson, 1954; Belsey, 1954). A case of hiatus hernia, weighing 13 lb. at 17 months of age, has recently been admitted to the Hospital for Sick Children, Toronto, with a virtually impassable stricture.

If vomiting diminishes one should not necessarily believe that all is well, because, paradoxically, decrease in vomiting may be due to the formation of a moderate stricture (Waterston, 1954) so that close control is advisable. The very long-term outlook is obscure. It is now well recognized that hiatus hernia is one of the commonest findings on barium-meal examination in adults (Allison 1951; Avery Jones, 1952; Hodgson, 1954). The following figures of incidence in adults having upper gastrointestinal series have recently been reported: Brick (1950) 8.93%, Pickard* 11%, and Evans (1952) 3%. Whether these are persisting or recurring hernias first present in infancy or childhood is unknown, and only very careful observation over a long period will tell.

Allison has demonstrated spontaneous reduction by means of metal clips placed on the esophagogastric mucosal junction. At subsequent screening the clips may be seen above and below the diaphragm at different times. It is possible that, in a proportion of cases, with the assumption of the upright posture, permanent reduction is achieved and, with increasing activity, growth, and muscular development, the hiatal and esophageal closing and tethering mechanisms become efficient resulting in permanent cure. However, Astley and Carré's (1954) impression is that, though symptomatic cure is usual, the partial thoracic stomach persists in nearly all, and this is my experience.

Another aspect of the disease affecting mortality, though this applies more particularly to adults, is the liability of patients with hiatus hernia to develop true peptic ulceration in the stomach, either above or below the diaphragm (Barrett, 1950, 1954) or in the duodenum.

Gastric ulceration was strongly suspected though not proved in the following case.

Report of Case

Case J. G.—This baby girl, with a proved hiatus hernia, suffered from increasingly severe, though intermittent, vomiting from birth. At 5 months there was an acute hematemesis together with melena. From then on vomiting continued with occasional blood-streaking. At 15 months of age, after a crying episode, the mother found a large blood clot in the child's mouth and fresh blood on the pillow. The child was esophagoscoped four days after this, but there was no evidence of esophagitis or stricture formation. The absence of esophagitis so shortly after a frank hematemesis strongly suggested peptic ulceration below the esophagogastric junction.

Cases of hiatus hernia often have a high acid curve in the stomach (Belsey, 1952). Barrett (1950, 1954) has distinguished between true peptic ulceration occurring on gastric mucosa above the diaphragm and reflux esophagitis with ulceration of the squamous epithelium of the gullet. There is a distinct danger of perforation or severe bleeding in these cases of true peptic ulceration. Frank hematemesis is more likely to be due to peptic ulceration than to reflux esophagitis, where blood streaking or coffee-ground vomiting is more usual.

SECTION VI—ESOPHAGEAL HIATUS HERNIA: CLINICAL FEATURES

Age and Sex Incidence

Figure 15 shows the age and sex incidence of the 17 cases in this series. The numbers are too small to point any sex trend, but they do indicate that the disease can, and should, be diagnosed at a tender age. The earliest diagnosis was made at 4 days of age by esophagoscopy; 3 were diagnosed at less than 12 days of age; 7 under 1 month; 13 under 6 months, and 15 under 1 year. Waterston

* Pickard, C.: M.D. Thesis, University of Leeds, cited by Johnstone, 1952.

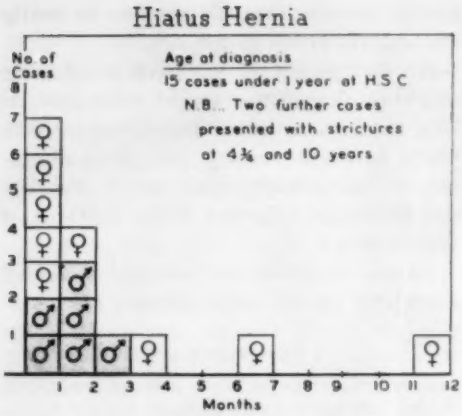

Hiatus Hernia
No. of Cases
Age at diagnosis
15 cases under 1 year at H S C
N.B... Two further cases presented with strictures at 4¾ and 10 years
Months

Fig. 15.—Age and sex incidence.

(1954) showed a roentgenogram of an infant of 3 days with a definite hernia, while Pilcher (1951) stated that he has seen several cases of hiatus hernia who vomited blood on the first day of life.

Avery Jones (1952) reported a sex ratio of three females to one male in 128 adult cases. Allison (1951) found two females to one male in 176 cases, and Rennie, Land, and Park (1949) two females to one male in 31 cases.

Signs and Symptoms

Table 2 shows the mode of presentation in the 17 cases in this series. Vomiting is the most frequent complaint bringing the case to notice.

Table 3 lists the four common clinical findings. Vomiting is constant, though other more dramatic features may sometimes thrust it from the limelight. Wasting and anemia are almost as invariable in cases of some standing, and the somewhat lower incidence in this series is due to the extreme youth of some of the cases.

Vomiting is usually present from birth. In the absence of esophagitis it does not distress, and the infant will recommence avid feeding if given the opportunity following a bout of vomiting. It may be persistent or recurrent, with intervals of freedom of days or weeks. Vomiting consists of feedings, usually mixed with much mucus, and occurs usually during or after feedings. It may be bile- or blood-stained. Projectile vomiting has been noted even in the absence of pyloric stenosis, which occasionally coexists. With the introduction of solids into the diet a reduction in vomiting may ensue, unless there is marked esophagitis or stricture formation, when an exacerbation may be expected with obvious dysphagia and regurgitation.

Profuse oropharyngeal secretions may cause difficulty with respiration and choking over feedings.

Constipation may result from low food and fluid intake.

Failure to gain satisfactorily is almost constant and varies directly with the degree of vomiting and feeding difficulty.

Hematemesis is usually confined to streaking or coffee grounds. It results from oozing over an area of reflux esophagitis. It was present in 8 of our 17 cases. There may be mild melena or occult blood in the stools.

Anemia of less than 11 gm. per 100 cc. occurred in 13 of our cases. In one it was present shortly after birth and was due to concomitant Rhesus isoimmunization. In the remainder the anemia was of the hypochromic microcytic type and was partly dependent on blood loss and partly on malnutrition. Thus, in 5 of the 12 anemic cases, clinically obvious hematemesis or melena was never recorded. The incidence of anemia among adult cases of hiatus hernia has been reviewed by Ritchey and Winsauer (1947).

Table 2.—*Hiatus Hernia—Leading Features of Seventeen Cases in Infancy and Childhood at H. S. C.*

Leading Feature		
Vomiting	10	
Choking over feedings	1	
Aspiration pneumonitis	2	
Incidental finding	1	(marked symptoms)
Emaciation	1	
Obstruction due to stricture	2	
	17	

Table 3.—*Seventeen Cases of Hiatus Hernia at H. S. C.—Clinical Features*

Cases	Vomiting	Wasting	Anemia <11 Gm./100 Cc.	Hematemesis
17	17	13	12*	8

* Excludes one case with anemia due to coincidental erythroblastosis fetalis.

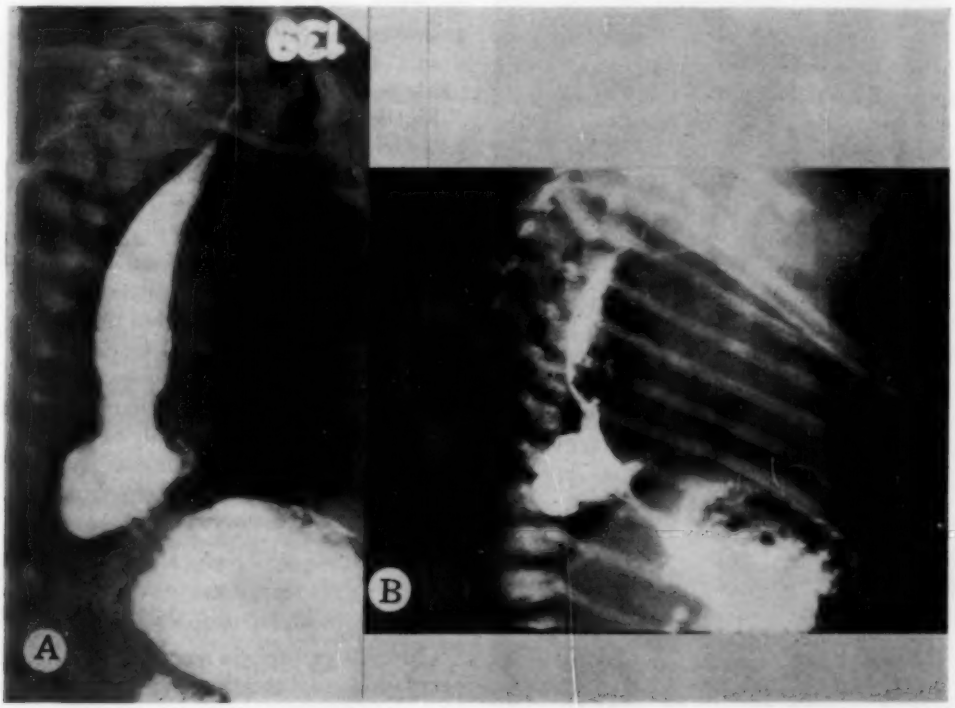
Belsey speaks of the inconstant relationship of pain to esophagitis as judged by esophagoscopy (1954) but Creamer (1955) was able to show that heartburn frequently followed within 30 seconds of reflux detected by pressure changes in the esophagus. The ill humor and intractability of some small infants with hiatus hernia may be the clue to the pain behind the lower sternum and dysphagia which older children and adults may complain of on swallowing over a raw area of esophagitis. Some infants learn to get relief from this discomfort by self-induced vomiting. Boring pain between the scapulae in adults indicates periesophagitis.

SECTION VII—ESOPHAGEAL HIATUS HERNIA: DIAGNOSIS

The first requisite is clinical suspicion, but confirmation is by radiology. Soresi (1919) made an eloquent plea for the more frequent recognition of diaphragmatic hernia and was the first to describe the technique of barium examination in the horizontal position essential to demonstrate reflux. This technique has been fully discussed in a number of papers referring to adults by Åkerlund (1926), Johnstone (1943, 1952), Bloom (1947), Stapleton (1947), and Evans (1952) and in children by Findlay and Brown Kelly (1931), Wamberg (1947), Thomsen, (1949), Astley and Carré (1954), and Hodgson (1954).

There are technical points of importance. The examination should always be made in the horizontal position in infants and children. An initial swallow of a thick bolus of barium will often be more informative than the use of a thin suspension, because a stream effect down one wall of a supradiaphragmatic pouch of stomach will be less likely to confuse (Fig. 16*B*). The bolus is often held up in the supradiaphragmatic pouch. Following this it is essential that the stomach be distended with a thin barium suspension (a 50% weight/volume suspension is recom-

Fig. 16.—Appearance of the barium-filled esophagus at different moments during the same examination. In *B* the stream effect gives a spurious impression of the presence of a stricture.



mended by Astley and Carré; sugar and dried milk may be added) given most conveniently in the case of infants from a feeding bottle. If abnormal reflux is not immediately obvious, it can usually be produced in the presence of a hernia by the rise in intra-abdominal pressure on crying, or external pressure on the abdomen. Raising the buttocks off the couch or the oblique prone position may help. These maneuvers are essential to fill the supradiaphragmatic pouch and to delineate the lower face of a possible stricture. Spot radiographs may show the presence of gastric mucosal folds above the diaphragm. Interpretation of irregularities in the barium outline is fraught with difficulty, and while it is sometimes possible to deduce ulceration or reflux esophagitis, such deductions should be checked with the esophagoscope.

Since in some cases the herniation is intermittent, or reflux may be difficult to produce because of relative competence at the diaphragmatic hiatus, a negative radiological result in the presence of a suggestive history should be treated with some reserve and the investigation repeated. In this series a barium swallow was passed as normal in two cases though subsequent examination in one showed one-third of the stomach in the thorax and in the second esophagoscopy revealed the gastroesophageal junction to be above the diaphragm.

Esophagoscopy

This investigation is essential to exact diagnosis of reflux esophagitis and ulceration and allows a stricture to be inspected and if necessary dilated. It is indicated, irrespective of age, whenever esophagitis or obstruction due to stricture or impaction is suspected. At the Hospital for Sick Children, Toronto, the situation of the gastroesophageal junction in relation to the diaphragm is assessed by fluoroscopy with the esophagoscope in situ.†

Differential Diagnosis

Distinction has to be made from other causes of vomiting and failure to thrive. These are such common symptoms in infants that the task might seem formidable. Clinical acumen is required, but careful attention to the history and character of the vomiting will permit selection of cases for further investigation.

In the neonatal period it is essential to exclude esophageal atresia or high intestinal obstruction. Though one case in this series, by reason of very profuse oropharyngeal secretions and choking over feeds, suggested this diagnosis, such severe symptoms in the immediate neonatal period are unusual in hiatus herniation. Vomiting due to congenital pyloric stenosis is unlikely before 3 or 4 weeks of age and is easily differentiated by feeling the tumor. It occasionally coexists with hiatus herniation (Pilcher, 1951; Waterston, 1954).

Vomiting from intracranial lesions will be differentiated on clinical grounds reinforced by special tests, such as lumbar or subdural puncture.

Infections of any sort, but chiefly otitis media and pyelitis, may give vomiting in infancy but should not cause diagnostic difficulty.

Later in infancy and childhood, metabolic disorders, such as infantile renal acidosis or galactosemia or the cyclical vomiting syndrome, should be differentiated by appropriate tests.

Finally, differentiation must be made between the common hiatus hernia and the rare developmental esophageal shortness. Where the latter takes the form of the gastric-mucosa-lined esophagus (Fig. 3*F*), the situation can be suspected from the esophagoscopic recognition of gastric mucosa extending to a very high level in the esophagus. Where the stomach and esophagus are normally differentiated morphologically (Fig. 3*G* and lined by their respective mucosae, the diagnosis can probably only be made at operation or necropsy by the assessment of the true shortness of the esophagus with absence of inflammatory fibrotic shortening.

Section VIII—Esophageal Hiatus Hernia: Complications

Dysphagia Pneumonitis

Chronic dysphagia in adults may result in overflow of esophageal content into the bron-

† Fearon, J. B.: Personal communication to the author, 1954.

chial tree with resulting pneumonitis (Belcher, 1949). Aspiration is a hazard even in normal infants, but the danger is definitely increased where regurgitation accompanies hiatus hernia. In addition, as a result of reflux, there is frequently a copious salivary and esophageal secretion (Aylwin, 1953) which may be aspirated from the oropharynx.

Report of Cases

Case G. S.—This baby girl was admitted at 16 hours of age. She was born at home and, in emergency, mouth-to-mouth inflation of the lungs was carried out. On starting oral feeds she choked and had a profuse mucoid oropharyngeal discharge. The breathing and cry were obstructive, but the infant was not cyanosed. A radiograph on the second day of life showed a segmental atelectasis on the right, with air in the anterior mediastinum and some surgical emphysema in the neck. On the third day of life laryngoscopy and bronchoscopy disclosed that the vestibular folds and vocal cords were red and swollen and that all major bronchi were filled with secretion which was sucked out. A tracheotomy was performed because of the laryngeal obstruction and also because it was judged easier to control the danger of further aspiration in this way. Esophagoscopy was also carried out on this day and showed the gastroesophageal junction to be above the diaphragmatic hiatus. The mucous membrane in this region was red, swollen, and covered with exudate.

Case G. H.—This baby girl was admitted on the first day of life as a severe case of erythroblastosis fetalis, which was successfully treated. The baby had been noted to have a profuse oropharyngeal secretion. There was a tendency to choke over feedings, and she was vomiting from two to seven times daily, the vomit being brownish and containing mucus on several occasions. She always had an obstructive cry and respiration. Because of this, laryngoscopy was carried out on the sixth day of life and showed milk curd and mucoid discharge in the oropharynx and above and around the cords. The aryepiglottic folds were swollen and inflamed. On the 12th day of life a barium swallow revealed a small hiatus hernia. No lung lesion developed in this child largely owing to the diligence of the nursing staff in sucking away secretions.

Case D. T.—This baby, admitted at 3 weeks of age, had lost 35 oz. from his birth weight. There had been constant feeding difficulty since birth, and in hospital the infant vomited from two to five times daily. Investigation revealed an Escherichia coli pyelitis which was treated. The intravenous pyelogram was normal. Vomiting continued, and a barium swallow at 4 weeks of age suggested obstruction at the lower end of the esophagus. The baby choked during the examination, and Figure 17 shows that there was overflow of barium into the bronchial tree. Because of physical signs of secretion in the chest, bronchoscopy was carried out three days later. Thick mucoid exudate was aspirated from all the major bronchi. An esophagoscope was then passed, and the gastroesophageal junction was seen to be at approximately the upper surface of the dome of the diaphragm under fluoroscope with the esophagoscope in situ.

Fig. 17.—Overflow of barium into bronchial tree during barium swallow in a case of hiatus hernia (Case D. T).

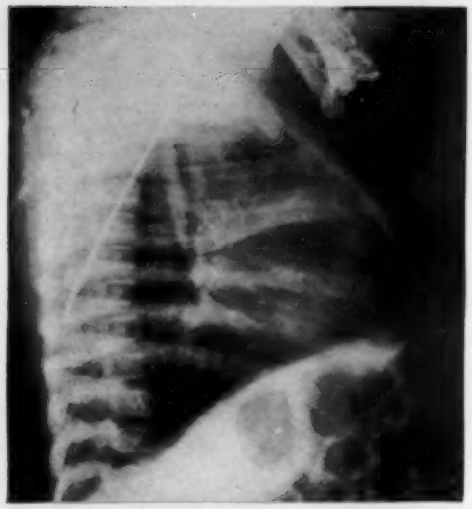


Fig. 18.—Aspiration pneumonitis of the anterior division of the right upper lobe (Case R. P).

Case R. P.—This boy was admitted at 11 weeks of age with a history of choking over feedings and a tendency to wheeze since birth, which wheezing was worse after feedings. The parents had noted much mucoid secretion. On admission there were physical signs of pneumonia, and the radiograph (Fig. 18) showed a segmental lesion in the right upper lobe. Subsequent barium swallow confirmed a hiatus hernia, and esophagoscopy disclosed superficial ulceration and slough on the left posterior aspect of the gastroesophageal junction, which was about 1 cm. above the hiatus.

These four cases were the most marked examples of respiratory difficulty in the series, but careful analysis of the histories showed that seven others had milder respiratory symptoms, probably referable to aspiration of excess seromucoid secretion or feedings. One case in the series (Case G. B.), the only example of developmental shortness of the esophagus, finally died of aspiration pneumonitis. While it is likely that gastroesophageal incompetence contributed to this mode of death, she also had multiple congenital anomalies, including a nuchal meningomyelocele.

The earlier literature contains reports of cases dying from aspiration or pneumonia (Bund, 1918; Beatty, 1928; Sheldon and Ogilvie, 1929). Belsey (1953) has recently emphasized again the danger of pulmonary atelectasis and fibrosis from recurring aspiration. It is conceivable that a number of deaths from this cause occur without the realization that there is an underlying hernia even after postmortem examination.

Acute Obstruction

Where a tight stricture has formed there is a danger of acute obstruction by impaction of food particles.

Report of Case

Case K. L.—This girl was admitted at 4¼ years of age, after a long history of intermittent dysphagia and vomiting. The previous week she had vomited "everything" and had been constipated for three days. On admission she weighed 23 lb. and was acutely ill and dehydrated. Intravenous fluids were necessary. Only 3 fluid ounces of milk was retained on the first day. Pureed foods were regurgitated shortly after they were swallowed. Esophagoscopy revealed a very tight fibrous stricture with a moderate degree of esophagitis above.

Sometimes in such cases esophagoscopy will reveal an impacted particle of food, such as a pea, which the patient is unable to dislodge by vomiting.

Periesophagitis

Severe inflammation of the esophagus due to reflux may eventually spread to involve the periesophageal tissues, causing pain between the shoulder blades. Inflammatory fixation of the esophagus occurs, and, in advanced or neglected cases, sinuses may form tracking into the mediastinum or lungs.

Inflammatory fixation of the esophagus is a source of surgical difficulty in reducing certain hernias. Dissection and freeing of the esophagus, even up to the arch of the aorta, may be necessary before the cardia can be reduced below the diaphragm. It is obvious that the thoracic approach should be preferred where there is reason to suspect periesophagitis.

Rarer Complications

Belsey (1952) mentions the possibility of duodenal obstruction, which was the indication for operation in two of his cases. This is presumably due to dislocation of the stomach and kinking.

Volvulus or incarceration of the stomach may occur, especially in the paraesophageal type of hiatus hernia.

The increased liability to true peptic ulceration and its complications has already been mentioned in the section on prognosis.

SECTION IX—MANAGEMENT OF HIATUS HERNIA

The objects in infancy and childhood are to control esophagitis by discouraging reflux and regurgitation and to maintain nutrition.

Management—Conservative Treatment

The upright posture discourages reflux and should be maintained for 24 hours a day for a prolonged period. Some form of wooden-box seat lined with sponge rubber or a plaster of Paris chair (Hill, 1953) or a suspensory harness can be used both in hospital and at home. Another method, suggested to me by Dr. Neil Begg, of New Zealand, is to suspend the infant by the lateral margins of the diaper on an inclined mattress (Fig. 19). Postural treatment alone usually results in cessation or marked diminution in vomiting, with ensuing weight gain.

If vomiting continues, thickening of the feedings further discourages reflux.

It is logical also to attempt to reduce stomach and reflux acidity by antacids.

Severe anemia may require transfusions. Milder cases should be treated with iron.

Results of conservative treatment in children have already been considered under the section on prognosis. The immediate results are usually excellent and are typified by the following case.

Report of Case

Case G. R.—This baby girl was admitted at 6 days of age because of persistent vomiting and dehydration. A barium swallow showed hiatus hernia. During the first three days in hospital there was repeated vomiting of feedings up to 10 times a day, and interstitial fluids were required. On the third day the infant was suspended in the upright position (Fig. 19). During the succeeding six days vomiting gradually decreased in frequency and amount, and weight gain started. By the end of six days vomiting had ceased. At the end of 29 days the infant had gained 2 lb. 2 oz.

Immediate results in the eight other medically treated cases in this series have been comparable. A detailed analysis is valueless because of the short observation period.

In a small proportion of cases, probably less than 15%-20%, conservative treatment will fail to control symptoms and further measures will be needed.

Fig. 19.—Suspension by the lateral margins of the diaper to discourage gastroesophageal reflux.

Management—Phrenic Paralysis

This procedure has achieved irregular results as a measure to prevent reflux.

Success appears to depend on raising the dome of the left diaphragm, which also raises the position of the fundus relative to the cardia. Soutter (1947) claims that as a result a sliding hernia could often be shown radiologically to be reduced. If reduction does take place, the reconstitution of the incisural angle would presumably once again result in a competent mucosal valve.

Collis, Satchwell, and Abrams (1954) have shown that the left phrenic nerve supplies the left half of the right crus in addition to the left leaf. These workers now advocate selective paralysis of the left dome by cutting the lateral division of the phrenic nerve leaving the anterior and posterior divisions intact, so preserving crural function. This is accomplished by incising the diaphragm obliquely backward and inward toward the hiatus up to the central tendon through a combined abdominothoracic incision (Collis, Kelly, and Wiley, 1954). Harrington (1955) performs a routine phrenic crush before elective repair and claims that it facilitates such repair. Sweet (1952) crushes the left phrenic nerve at operation.

Harrington (1955) is of the opinion that it is a palliative measure and should not replace operative repair. He advises permanent paralysis in many cases of congenital short esophagus or in palliation where the general condition does not permit of operative repair of a hiatus hernia. He reported that approximately 45% of his 39 adult patients obtained marked to moderate relief, 40% were partially relieved, and 15% had no relief where phrenic paralysis alone was used.

Childhood experience of therapeutic phrenic paralysis is very meager. Husfeldt (1953) reported two infant cases of Dr. Petterson's and three of his own, all infants, who have responded well to phrenic crush. Dr. Petterson's cases are symptomatically and radiologically cured three years two months and two years eight months later, respectively. while his own cases showed dramatic improvement over a short period of follow-up.

Since Husfeldt's experience in infants it is possible that small sliding hernias may be permanently reduced after a phrenic crush, but it is probably impossible to know in advance which cases may benefit, and the risks of esophagitis are ever present. For this reason this procedure is not recommended for most cases which do not respond to medical treatment.

There is no place for permanent phrenic interruption in infancy or childhood because of the resulting interference with respiratory function. There is probably only a limited place for it in poor-surgical-risk adults. Phrenic evulsion is not without risks, as Amendola's (1955) case report of obstruction due to sharp angulation of the lower esophagus around the hiatal margin showed. This case, a 55-year-old woman, also suffered considerable respiratory embarrassment. On the other hand, Pickhardt, Rafsky, and Ghiselin (1950) reported good results from phrenic paralysis in a group of 29 elderly patients.

Management—Surgical Repair of Hernia to Control Reflux Esophagitis

If after a few weeks of adequate conservative treatment vomiting continues, weight is lost or not gained, and especially if the vomit contains blood, the case should be reassessed, such reassessment to include esophagoscopy. If there is continuing esophagitis, operation should be advised to forestall stricture formation. The decision is often difficult to make in individual cases, especially with our present incomplete knowledge of the natural history of hiatus herniation and its sequels. Accurate endoscopic assessment is of the greatest help combined with the clinical condition.

Eight cases in this series have been operated on, six through the abdomen and two through combined abdominothoracic incisions. There have been good immediate results in all cases as regards cessation of vomiting, cure of esophagitis, and subsequent weight gain. One case, operated on through a combined incision, recurred in the immediate postoperative period but had symptomatic improvement. A second, operated on through the abdomen, had clinical recurrence

eight months postoperatively, with return of blood-stained vomiting. The remaining six cases are doing well over a short period of observation up to one year. There has been no operative mortality or important postoperative complication.

Management—Cases with Stricture: Dilatation

The formation of a stricture may protect partially against further reflux, but the patient starves. Dilatation allows the patient to eat, but may once again permit reflux, with further esophagitis and aggravation of the stricture. Moreover, in a large proportion of cases with stricture, there is continuing ulceration, which requires treatment in addition to the stricture. To illustrate the situation which may arise following exclusive treatment by dilatation I will quote in full Belsey's experience of a childhood case (Belsey, 1952).

> In one case dilatation had been adopted as the method of choice for relieving the dysphagia. The stricture had been dilated under general anaesthesia every month or two until the child, a girl, was eight years old. She was then taught to pass a bougie upon herself every morning before breakfast. By the age of fifteen years, the child was undernourished, a psychological wreck, and swallowing with difficulty through a rigid tube of fibrous tissue, completely devoid of any mucosa. The resection of the stenosed oesophagus together with the upper half of the stomach followed by an oesophagogastric anastomosis at the level of the aortic arch have completely relieved the dysphagia and malnutrition and have been instrumental in the return of the girl's mental state to normal.

One must agree with Belsey's (1952) statement that such a case, and also the one from the same article, illustrated in Fig. 14, offer scant hope of satisfactory relief of dysphagia by dilatation. Dysphagia is, in any case, according to Belsey, not dependent solely on obstruction by the stricture but is also occasioned by loss of neuromuscular function by the rigid fibrosed esophagus.

Treatment by dilatation still carries the possibility of perforation, though happily the days of blind bouginage are over. The method of retrograde dilatation via a gastrostomy advocated by Tucker, Lautz, Tracy, and Fearon (1950) may be safer and effective.

Dilatation is at best a palliative and usually needs to be continued at intervals over a long period. But it is possible that a case of hiatus hernia with initial reflux and stricture formation may later acquire cardioesophageal competence. Aylwin's (1953) and Creamer's (1955) work, already referred to, suggests that only a minority of cases have persistent reflux in adult life. May it not be, therefore, that some cases without too severe a stricture may be satisfactorily, and more or less permanently, treated by dilatation? Perhaps it will be possible in the future, by the application of the methods in use by Creamer and Aylwin, to pick out such cases for treatment by dilatation, while passing on those cases with persistent ulceration and reflux for repair or resection.

Management—Cases with Stricture: Repair and Subsequent Endoscopic Dilatation

In 1951 Pilcher reported the case of an 8-week-old boy with cured congenital pyloric stenosis and a hiatus hernia who developed a stricture. Operative repair of the hernia was carried out, and the stricture subsequently dilated endoscopically. Five months later there had been no recurrence of vomiting and the infant was taking his feedings without difficulty.

This is a very useful method of treatment. Dilatation may need to be repeated on several occasions at increasing intervals but can usually be discontinued, since reflux esophagitis will in most cases have been prevented by hernial reduction. Carver and Sealy (1954) reported five cases where postoperative oral dilatation produced a satisfactory result, but they do not state how long the cases were followed.

Barrett (1954) on the other hand, denied that competence could be restored by hernial repair following reflux esophagitis and stricture formation. He contended that inflammation will destroy the presumed mucosal valve on which competence depends. This has not been my experience, but the question remains to be settled by further observation. There seems little doubt that most cases with an annular stricture where there has not been

too much periesophagitic fixation and fibrotic shortening of the esophagus can be operated on successfully and the cardia restored below the diaphragm. Some mobilization of the esophagus may be required.

Where difficulty has been experienced in reducing the cardia below the diaphragm, some surgeons have adopted the device of anterior displacement of the hiatus to a higher level on the dome. Merendino, Varco, and Wangensteen (1949) used this operation as their standard technique for repair of a hiatus hernia and reported no recurrences in 13 cases. They did not give details of their symptomatic results. Harrington (1955) believed it important to have at least 2 cm. of the esophagus below the diaphragm and often found it necessary to reform the hiatus at a higher level to achieve this object. Harrington did not state the number of cases in which this procedure was carried out, nor did he analyze the results separately.

Nicholson (1952) also used this method in an unstated number of his earlier repairs but cited it as an unphysiological operation and was surprised that the results had not been bad.

In line with recent thinking, the reconstitution of the angle of esophageal entry at a higher level may allow reformation of the mucosal valve and thus the regaining of cardial competence. There are insufficient reported data to evaluate this procedure, but the operation is not generally popular.

Management—Cases with Severe or Long Stricture

Where there is a severe stricture, some form of plastic procedure with resection is necessary. Removal of the acid-bearing portion of the stomach and anastomosis of the remainder to the lower end of the esophagus after resecting the stenosed segment is one possibility (Belsey, 1954).

Allison (1953) and Barrett (1954) preferred an esophagojejunostomy, excluding the stomach, following resection of the stricture. Even with this operation the risks of reflux esophagitis are not entirely eliminated, since there is a possibility that succus entericus may reflux. Carver and Sealy (1954) reported this complication in 3 of their 12 cases of esophagojejunostomy. Allison's paper should be consulted for technical details.

These operations could also be adapted to deal with cases of developmental shortness of the esophagus where ulceration of gastric mucosa or, more rarely, reflux esophagitis are problems.

Management—Cases of Paraesophageal Rolling Hiatus Hernia

There seems general agreement that the presence of a paraesophageal hernia is an absolute indication for operative repair because of the additional dangers of volvulus, incarceration, ulceration, and its complications of hemorrhage, perforation, and hourglass contracture.

Management—The Operation for Repair of Hiatus Herniation

Soutter (1947) mentions that the first operative repair of a hiatus hernia was carried out at the Massachusetts General Hospital in 1920 but gives no details of indications or technique.

In 1925, Strauss and Hess reported three infant cases operated on from 1921 onward. They mobilized the esophagus, reduced the cardia below the diaphragm, and dilated strictures at the lower end of the esophagus by retrograde traction bougies, introduced through the stomach wall. One case was doing well at the end of a two-year follow-up. The second died of postoperative pneumonia. The third "recovered." It is probable that these are the first reported cases of operative reduction of hiatus hernias in infancy. The authors did not, apparently, recognize what was presumably an underlying hiatus hernia, and the operation was undertaken to dilate the strictures from below. It is likely that the cardia was fixed in its normal position by postoperative fibrosis, thus resulting in cure.

This is not the place for a detailed consideration of the techniques of operation for repair of hiatus hernia. These are adequately

covered by Allison (1951), Belsey (1952), Husfeldt (1953), Collis, Kelly, and Wiley (1954), and Harrington (1955).

The technical and other problems involved in resecting strictures are likewise discussed by Allison (1953), Barrett (1952, 1954) and Belsey (1952, 1953, 1954). From an examination of the opinions of a number of practicing surgeons, the following principles underlying the performance of a successful repair may be stated.

1. Reduction of the cardia below the diaphragm, a procedure which results in reconstitution of the incisural angle.

2. Fixation of the cardia and fundus of the stomach to the under surface of the diaphragm (Fig. 10).

3. Narrowing of the hiatus by loose stitching, either anteriorly to increase the incisural angle (Collis, Kelly, and Wiley 1954) or posteriorly (Allison, 1951).

To these some would add the following:

4. Left phrenic paralysis, selective (Collis and others 1954) or total (Husfeldt, 1953, and Harrington, 1955).

Where there is a residual stricture, the following principle could be added:

5. Endoscopic postoperative dilatation (Pilcher, 1951).

Management—Repair of Hiatus Hernia: Operative Approach

During the early days of operation on hiatus hernias the abdominal route was most popular and still is largely, but not exclusively, preferred by Harrington (1955). During recent years there has been an increasing tendency to operate through the thorax (Soutter, 1947; Allison, 1951; Belsey, 1952; Waterston, 1954). Collis, Kelly, and Wiley (1954) now use a combined abdominothoracic incision, while others (Belsey, 1952, and Harrington, 1955) find it useful in selected cases.

Choice of route must be, to some extent, personal to the surgeon, but there are circumstances where one or the other route is obviously preferable. For example, coexisting abdominal disease, such as gallstones in the adult, will call for laparotomy, while evidence for periesophagitis will require the thoracic approach, since the esophagus will need to be dissected from the mediastinum.

There has been an increasing tendency for thoracic surgeons to operate on cases of hiatus hernia, and their approach has somewhat naturally tended to be thoracic. There are however, good reasons for the preference, and these have been well summarized by Belsey (1952) as follows:

1. Adequate exposure of the herniated stomach and esophagus, which can be freed from the mediastinum under direct vision if necessary.

2. Evaluation of any true or apparent shortening of the esophagus.

3. Ease of access for repair of the posterior margin of the hiatus by approximation of the crural fibers behind the esophagus.

4. Can be extended easily into a combined abdominothoracic approach if necessary.

5. Lower incidence of postoperative chest complications by interfering less with cough mechanisms.

6. Possibly a lower recurrence rate.

To these may be added the fact that infants and children stand thoracotomy extremely well, probably better than laparotomy.

The results of published series of operations on hiatus hernia have been summarized in Table 4. It is difficult to compare results, since indications for operation, age groups, techniques, length of follow-up, and methods of assessment differ widely. There is no doubt that surgery in selected cases is curative and in others relieves severe symptoms. In the presence of a severe stricture or in complicated cases of paraesophageal hernia, it can be life-saving.

Summary

During the last few years a new syndrome characterised by partial dislocation of the stomach into the thorax has become recognized in infancy and childhood.

This syndrome comprises two groups of cases, differing in frequency, pathogenesis, and management. These groups are (1) partial thoracic stomach due to developmen-

TABLE 4.—*Abstract of Published Results of Surgically Treated Cases of Hiatus Hernia*

Author and Year	Cases		Operation		Technique*	Follow-up	Assessment	Results	Remarks
	No.	Per Cent	No.	Per Cent					
Soutter, 1947	67	...	67	..	25 abdominal repair; 10 recurrences (x-ray proved)	1 yr.+	Clinical, x-ray	Symptoms relieved wholly or partly, 30	Age group not known, probably adults; death due to infection following cholecystectomy and herniorrhaphy; first operation performed in 1920; earlier operations were abdominal; since 1940 increasing use of transthoracic route
					37 transthoracic; 6 recurrences (x-ray proved)	1 yr.+	Clinical, x-ray	NK or followed <1 yr., 26; unimproved, 10; death, 1; final known recurrence, 18	
					5 phrenic crushes; temporary relief, 3; NK, 2	1 yr.+	Clinical, x-ray	NK, 2; recurrence of symptoms and herniation, 3	
Allison, 1951	176	100	33	19	Transthoracic repair; fixation of phrenoesophageal ligament; posterior repair of crura	Up to 5 yr.	Clinical, x-ray	Cured, 30; recurred, 1; symptoms, 1; death (coronary thrombosis 6th postoperative day), 1	Mostly adults
			15	8.5	Resection of stenosed segment and esophagojejunostomy	Up to 5 yr.	Clinical, x-ray	Cured, 15; deaths, 0	
Belsey, 1952	94	...	54	..	Transthoracic herniotomy, posterior repair of hiatus; fixation of cardia to hiatus	NK	NK	NK	Includes 14 cases in children; this series was reported to illustrate indications for operation rather than to asess results
	..	...	54	..	Resection of stricture, partial gastrectomy, and esophagogastrostomy	NK	NK	NK	
	..	...	2	..	Preliminary gastrostomy	NK	NK	NK	
	..	...	1	..	NK	NK	NK	NK	
Nicholson, 1952	62	100	32	51	Transthoracic herniotomy; 10 anterior displacement; 22 suturing right crus; 12 of 32 had phrenic crush	"Short"	Clinical	Good, 26; unsatisfactory, 3; recurrence, 1; died, 2	Adults; 1 death from carcinoma of cardia; 1 death (4th day) pul. embolus
Sweet, 1952	111	100	109	..	Obliteration of sac; reduction of hernia; repair of hiatus	6 mo.+	Clinical, x-ray in 10	Cure, symptomatic, 94; some improvement, 10; no improvement, 1; recurred, 2; NK, 2; postoperative deaths, 0	Adults; cured group includes 3 with congenital short esophagus; in the 10 with some improvement were 2 "neurotic" and 1 cong. short esophagus; the 1 with no improvement had carcinoma of head of pancreas

Husfeldt, 1953	19	...	19	..	Reduction of hernia; crura stitched to wall of esophagus; transthoracic route (technique [a])	NK	Clinical, x-ray	Cured, 7; recurrence, 10; stenosis, 1; NK, 1; deaths, 0	Children; many in this series had "considerable stenosis when operated on"
	8	...	8	..	Transthoracic herniotomy; esophagus stitched to cardia; fundus sutured to diaphragm; crura narrowed (technique [b])	NK	Clinical	Cured, 3; recurrence, 3; stenosis, 2; deaths, 0	
	21	...	21	..	Technique (a)	NK	Clinical, x-ray	Cured, 12; recurrence, 9	Adults
	26	...	26	..	Technique (b)	NK	Clinical, x-ray	Cured, 19; recurrence, 5; death, 1; NK, 1	Adults; death from pulmonary embolism; 17 sliding hernias, 4 recurred; 9 paraesophageal, 1 recurred
Belsey, 1954	20	...	20	..	Resection of stricture and part of stomach; esophagogastrostomy	NK	NK	Good, 19; death, 1	All severe strictures in children under 10 yr.
Collis, Kelly, and Wiley, 1954	35	...	35	..	Laparotomy repair	Up to 6 yr.	Clinical, x-ray	Improved, 23; recurred, 6; op. death, 1; unrelated death, 1; NK, 3; symptoms, 1	Age group NK, probably mostly adults
	18	...	18	..	Abdominothoracic repair; selective L phrenicotomy; anterior repair of hiatus; anchoring of fundus	3 mo.+	X-ray	Improved, 15; NK, 3; recurred, 0; deaths, 0	Age group NK, probably adults
Waterston and Pilcher (Waterston, 1954)	132	100	62	47	15 cases "early technique"; remainder "modified technique"; all transthoracic	11 recent; 51, 6 mo.+	Clinical, x-ray	Good, 32; fair, 11; unchanged, 8; recurred, 6; deaths, 0	Children; ½ of operated cases had stricture; 3 recurrences in first 15 cases after which technique modified
Harrington, 1955	489	100	450	..	Abdominal approach; herniotomy; repair or construction of new hiatus; cardia fixed to diaphragm	NK	NK	Apparent cure, 437; recurred, 13; deaths, 6	Ages not given, presumably mostly adults; in 29 cases other operative procedures in addition to hernial repair necessary; 1 death in this group; details of follow-up examinations not given
	..	...	39	..	Phrenic crush or evulsion	NK	NK	Marked to mod. relief, 45%; partial relief, 40%; no relief, 15%	Palliative procedure procedure either because patient in poor condition or because hernia small

* NK indicates not known.

tal shortness of the esophagus, and (2) partial thoracic stomach due to herniation through the esophageal hiatus of the diaphragm. Contrary to what has been believed for many years, cases of esophageal hiatus herniation far outnumber those with congenital shortness of the esophagus. This paper examines the evidence on which this distinction has been made.

The several varieties of each group are described.

The pathogenesis of hiatus hernia is examined in detail particularly with regard to the mechanisms of fixation of the cardiac, which can be shown to be deficient in many cases. Reflux of gastric contents and consequent esophagitis is the chief hazard, and recent work is cited suggesting that the primary agent of competence at the cardiac is a mucosal valve and not a sphincter. When the angle of entry of the esophagus into the stomach is lost, as it is in hiatus herniation, incompetence of this valve results in a proportion of cases.

The chief results of this incompetence are esophagitis, stricture formation, and malnutrition, but dysphagia pneumonitis and anemia are also significant sequels.

The natural history of hiatus hernia is examined, and prognosis is considered, with particular reference to stricture formation and other complications. In 1177 published cases of hiatus hernia of all age groups the incidence of stricture formation was 17.7%. Remaining cases appear to lose their symptoms though not their herniae. In infants there is usually a great improvement with weaning onto solids.

The common clinical features are vomiting, wasting, anemia, and hematemesis. It is pointed out that the diagnosis can and should be made during the first few months or even weeks of life.

The diagnosis is made by clinical suspicion, radiology, and esophagoscopy. The special technique necessary for radiological diagnosis is discussed. The esophagoscope is indispensable in assessing esophagitis and its response to treatment and is frequently useful in diagnosis.

Differential diagnosis is considered briefly and is chiefly that of vomiting in the early months of life.

Methods of differentiating developmental esophageal shortness from hiatus herniation are mentioned.

Management is directed at preventing gastroesophageal reflux, which controls vomiting and forestalls esophagitis and stricture formation.

This is achieved conservatively by maintenance of a nearly upright position throughout the 24 hours, reinforced by thickened feedings and antacids.

Where conservative treatment does not rapidly control gastroesophageal reflux, operation to repair the hernia is advised. The paraesophageal hernia is considered an absolute indication for operation.

The indications for, and effectiveness of, various surgical treatments are assessed, including repair, phrenic paralysis, endoscopic dilatation, and resection of strictures.

The principles of surgical repair are stated with regard to the pathogenesis already described. The most important of these principles is the reformation of the angle of entry of the esophagus into the stomach by fixation of the stomach and cardia in their normal positions below the diaphragm. This enables the presumed mucosal valve to function efficiently again.

The treatment of cases with stricture solely by endoscopic dilatation is discussed but condemned except under special circumstances which are enumerated. A few cases will require resection of the stricture and gastrojejunostomy or partial gastrectomy and anastomosis of the remaining stomach to the residual esophageal segment in the thorax.

The comparative advantages of the abdominal and thoracic operative approaches are discussed.

The published surgical results of the larger series in the literature are summarized in Table 4.

Many of the points made in the paper are illustrated from a series of 18 cases seen per-

sonally at the Hospital for Sick Children, Toronto, during a recent 18-month period.

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Dr. J. D. Munn and the staff of the Department of Radiology provided access to radiographs.

Miss Marguerite Drummond and the staff of the Department of Visual Education prepared the illustrations.

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News and Comment

PERSONAL

Appointment of Dr. Frank Falkner.—The University of Louisville; from January, 1956. Dr. Frank Falkner has been appointed assistant professor of child health. Dr. Falkner is at present lecturer in child health, The Institute of Child Health, The Hospital for Sick Children, Great Ormond Street, London, and research assistant to that hospital. He is also coordination officer to the *Centre International de l'Enfance*, Paris, for their coordinated growth studies. These studies, taking place in different countries, have, as yet, no North American member of the "group." It will be part of Dr. Falkner's duties to set up such a cooperating growth study in Kentucky, and he will keep his appointment in Paris.

Appointment of Dr. Blair Batson.—Dr. Blair Batson has been named professor of pediatrics and chairman of the department of pediatrics at the University of Mississippi School of Medicine.

For the past year he has been assistant professor in both child health and pediatrics at The Johns Hopkins University School of Medicine.

GENERAL NEWS

Heinz Laboratory of Children's Hospital.—A gift of $500,000 has been made by the H. J. Heinz Company Foundation, the Howard Heinz Endowment, and H. J. Heinz II to Children's Hospital of Pittsburgh for the establishment of research chemical laboratories which will be known as the Heinz Laboratory of Children's Hospital.

In announcing this gift Mr. Heinz said, "The work of Children's Hospital in increasing its outpatient services, its educational program, and its pediatrics research deserves the admiration and support of every Pittsburgh citizen. The importance of laboratory work in our own business made it seem that the creation of a thoroughly equipped laboratory would be the most appropriate type of gift we could provide for Children's Hospital to assist it in attaining the immense objectives it has set for itself."

The Heinz Laboratory is to be a part of a new building now being planned.

ANNOUNCEMENTS

Fellowship in Pediatric Cardiology.—A Fellowship in Pediatric Cardiology under the auspices of the American Heart Association (Colorado Chapter) is now available at the Children's Hospital in Denver. Facilities and supervision are excellent; clinical material is abundant. Children's Hospital is a 210-bed fully accredited institution that has been actively engaged in cardiac diagnosis and treatment for many years. Graduates of Class A medical schools who have satisfactorily completed one or two years of hospital work are eligible. The stipend is $3600 per annum. Communicate at once with the Director, Cardio-Pulmonary Laboratory, Children's Hospital, Denver 18.

Abstracts from Current Literature

Prematurity and Congenital Deformities

CONGENITAL DEFORMITIES IN CHILDREN OBSERVED OVER A FIVE-YEAR PERIOD IN THE CHILDREN'S HOSPITAL OF ALEXANDRIA. G. CANESTRI, Lattante **25**:415 (July) 1954.

Data are presented as to the incidences of three congenital conditions—dislocation of the hips, deformed feet, and torticollis—in the city of Alexandria and its environs.

One or more of these deformities was found in about 1 of every 200 newborn infants. The incidence of congenital dislocation of the hip was 4.3 times as frequent in girls as in boys. The three essential points in the therapeutic management of congenital dislocation of the hip are early diagnosis, early treatment, and follow-up care.

Of the foot deformities, 48% were talipes valgus, 36% talipes varus (club foot), and 10% in the metatarsal arch. Twelve per cent of the cases of congenital dislocation of the hip had deformities of the feet or torticollis. Thirty-three per cent of the infants with torticollis had one of the other two deformities.

HIGGINS, Boston.

PROBLEMS IN THE TREATMENT OF PREMATURE INFANTS. W. TOBLER, Acta pediát. españ. **12**:565-571 (July) 1954.

The author gives statistical details on premature infants at the cradle home in the Canton of Berne in Switzerland. He discusses the question of incubators and the possibility of the use of Laborit's artificial hibernation which reduces the need for oxygen to the tissues and the prevention of irreversible shock. (Many of these children, however, are already in shock at birth.) He also discusses the use and abuse of oxygen and the prevention of infections in the newborn infant.

ALLEN, Santa Fe, N. Mex.

PARTIAL SEQUELA OF RETINOPATHY OF PREMATURE INFANTS (RETROLENTAL FIBROPLASIA). MARCEL LELONG, ALFRED ROSSIER, and MARTINE FONTAINE, Rev. españ. pediat. **10**:369-376 (May-June) 1954.

The authors, in studying 10,001 premature infants weighing less than 2000 gm., found 136 children with retrolental fibroplasia or the evidence of a regression of the process. While 5% had complete retrolental fibroplasia, the other 95% showed evidence of healing of the process. They describe the stages in development and hazard no guess for the cicatrization which in some cases merits a better prognosis in 95%.

ALLEN, Santa Fe, N. Mex.

PAPER CHROMATOGRAPHY IN GARGOYLISM. H. SCHOENENBERG, Monatsschr.. Kinderh. **102**: 404-407 (Sept.) 1954.

Two children with gargoylism were found to have aminoaciduria by means of paper chromatography studies. Pathological amino acids noted in the urine chromatogram were valine, tryptophan, leucine, phenylalanine, tyrosine, arginine, proline, and cystine. Peripheral blood smears and bone marrow examinations did not reveal Alder granulations of leucocytes.

Two other children with gargoylism whose leucocytes did show Alder granulations did not exhibit pathological aminoaciduria by paper chromatography.

HARTENSTEIN, Milwaukee.

Newborn

NEONATAL GROWTH IN WEIGHT OF NORMAL INFANTS OF FOUR DIFFERENT FEEDING REGIMENS. WILLIAM L. NYHAN and MORRIS A. WESSEL, Pediatrics **14**:442 (Nov.) 1954.

Neonatal weight changes of 400 normal infants were studied statistically. The series was composed of 200 infants fed on a flexible schedule, 100 of which were breast-fed and 100 bottle-fed, and 200 infants fed on the conventional four-hour schedule, 100 of which were breast-fed and 100 bottle-fed. During the first week of life the ad-lib-fed babies had smaller weight losses

than the schedule-fed babies, and the bottle-fed babies had smaller losses than the breast-fed babies. The duration of weight loss was longer in the breast-fed babies. By the time of the six-week postnatal clinic visit, the group that had been breast-fed in the nursery had gained significantly more than the group that had been bottle-fed in the nursery. There were otherwise among the four groups no significant differences in weight gain during this period. It was felt that the observed differences among the four groups paralleled the expected differences in food intake.

FROM THE AUTHORS' SUMMARY.

THE FIRST TEN MINUTES. H. B. ATLEE, Canad. M. A. J. **71**:227-234 (Sept.) 1954.

The author, an obstetrician, presents a plea for more careful consideration of the first 10 minutes of a baby's life. He feels that proper supervision by the obstetrician means careful and constant surveillance for at least 10 minutes, rather than merely accepting a first cry. He believes that five minutes by the clock is required for adequate drainage of amniotic fluid from the air passage and that this should be done with the baby in a head-down position. This procedure becomes especially important following Caesarean section.

The responsibility for the welfare of the infant is the obstetrician's and should not be delegated to a nurse or intern.

McGUIGAN, Evanston, Ill.

A B O BLOOD GROUPS AND FOETAL ERYTHROBLASTOSIS. ELIZABETH K. TURNER, M. J. Australia **2**:340-342 (Aug. 28) 1954.

A B O incompatibility is becoming a commoner and commoner cause of erythroblastosis in the newborn. The A B O titer is frequently sharply increased during pregnancy. Determination of such a titer rise is much more difficult than the usual RH titer determination. Useful techniques for this procedure have been developed, and studies have been made. They revealed 35% incompatible ratings, as against 13% for the RH factor. Fifty per cent of the first-born infants of the A B O incompatibility groups were affected. On these the Coombs test was negative. Transfusions in the mother apparently did not have any effect on the A B O group.

The author's figures revealed that the chance of RH sensitization is about half that of A B O sensitization. However the chance of the infant being affected in the A B O group is only about one-fifth of that in the RH group.

McGUIGAN, Evanston, Ill.

PREVENTION OF HYALINE MEMBRANE AFTER CAESAREAN SECTION. JUNE PASH, M. J. Australia **2**:386 (Sept. 4) 1954.

Aspiration of the mouth and pharynx immediately on exposure of the face during Caesarean section has seemed to be a logical means of preventing formation of pulmonary hyaline membranes. In 60 cases no deaths have occurred from this cause with use of this technique.

McGUIGAN, Evanston, Ill.

PULMONARY HYALINE MEMBRANES IN THE NEWBORN. K. R. HARNAES and K. H. TORP, Arch. Dis. Childhood **29**:199 (June) 1954.

An analysis is given of 56 infants with pulmonary hyaline membranes examined post mortem. The findings indicate that the first day of life is especially critical in infants presenting this syndrome. Most infants with hyaline membranes who died after the first day of life presented severe accompanying lesions at necropsy.

Before death, a marked disproportion between the exaggerated respiratory movements and the diminished breath sounds was found to be an outstanding feature.

KELLY, Milwaukee.

CONGENITAL LOBAR EMPHYSEMA. R. H. WHITE-JONES and L. J. TEMPLE, Arch. Dis. Childhood **29**:248 (June) 1954.

A case of congenital lobar emphysema occurring in a newborn infant is described. A diaphragmatic hernia as an associated defect was also present.

The importance of early recognition of the condition is emphasized, as these cases tolerate lobectomy well. The operation is a life-saving measure.

The symptoms are fairly constant and characteristic, and it is suggested that when an infant previously well and with no evidence of infection has attacks of dyspnea and cyanosis, congenital lobar emphysema should be considered.

KELLY, Milwaukee.

THE PROGNOSTIC SIGNIFICANCE OF NEONATAL CONVULSIONS. JOYCE B. BURKE, Arch. Dis. Childhood **29**:342 (Aug.) 1954.

The purpose of this study was to determine the prognostic significance of neonatal convulsions.

There were 48 cases in 8679 deliveries (0.2%). Eighteen infants (37.5%) died within a few days of birth. One infant was born with hydrocephalus and spina bifida. The remaining 27 infants were followed up. Five were severely retarded mentally; spastic quadriplegia was present in one of these, and further convulsions had occurred in two; a sixth child was blind in the left eye.

Convulsions were associated with birth trauma or anoxia in 35 cases (70%).

KELLY, Milwaukee.

Acute Contagious Diseases

MEASLES ENCEPHALITIS: A SUCCESSFUL METHOD OF TREATMENT WITH TYPHOID VACCINE. EVELYNNE G. KNOUF and ALBERT G. BOWER, California Med. **81**:18 (July) 1954.

During a 12-year period 50 patients with measles encephalitis were treated with typhoid vaccine—45 of them not until they were in a vegetative state. There were no deaths in the treated cases. All except one were clinically normal after treatment was ended. Late in the series it became apparent that after the clinical normal is attained and the electroencephalogram becomes normal, treatment should still be continued until the cortex has been "challenged" repeatedly and the electroencephalogram shown to remain normal.

The "shock" element in the treatment with typhoid vaccine was prevented by anticipating and circumventing the unfavorable reactions to the vaccine.

It may take 20 to 50 treatments or more with typhoid vaccine to return a patient to normality. Each individual is different and responds in a different period of time.

PRYOR, Redwood City, Calif.

ABSENCE OF TONSILS AS A FACTOR IN THE DEVELOPMENT OF BULBAR POLIOMYELITIS. GAYLORD W. ANDERSON, and JEANNE L. RONDEAU, J. A. M. A. **155**:1123 (July 24) 1954.

The authors state that more persons with bulbar poliomyelitis have had their tonsils out than those with the spinal form. If clinically recognizable poliomyelitis develops in a person who has had his tonsils removed the likelihood of bulbar involvement is four times as great as in one whose tonsils are in situ. The higher proportions of bulbar involvement in older persons and in recent years is due to a greater incidence of tonsillectomies.

KIMBALL, Evanston, Ill.

THE EFFECT OF PENICILLIN UPON THE VIRULENCE OF C. DIPHTHERIAE. MARY GIBLIN and HENRY BAUER, Minnesota Med. **37**:577 (Aug.) 1954.

The bacteriostatic effect of penicillin in six strains of virulent Corynebacterium diphtheriae was demonstrated by the failure to produce visible growth after 48 hours of incubation. If these apparently nonvisible cultures were then transferred to Löffler's medium, abundant growth with typical morphology was obtained.

The authors concluded that the virulence of C. diphtheriae is not lost by partial or apparently complete bacteriostases induced by penicillin.

It is reasonable to assume that patients whose cultures are negative during antibiotic therapy may harbor virulent C. diphtheriae after therapy is terminated. Cultures taken for the purpose of releasing patients from restrictions should be taken no earlier than 48 hours after discontinuance of antibiotic treatment.

STOESSER, Minneapolis.

USE OF ERYTHROMYCIN IN DIPHTHERIA. JAMES F. BLUTE JR., New England J. Med. **251**:71 (July 8) 1954.

The author treated three cases of acute pharyngeal diphtheria and one case of diphtheria carrier state with erythromycin. Antitoxin was given to two of the acute cases in addition.

The organisms were cleared from the nose and throat within 24 hours, and repeated cultures were negative. The case reports are given and the routes of administration described.

Erythromycin is advocated as an adjunct and not a substitute for antitoxin in cases of acute pharyngeal diphtheria.

WHEELOCK, Denver.

SECOND ATTACK OF POLIOMYELITIS. SCOTT B. MCKEOWN, Northwest Med. **53**:1119 (Nov.) 1954.

A case report is presented of a 34-year-old woman who suffered two attacks of clinical paralytic poliomyelitis 19 months apart.

The author has been able to find only two other reported cases with duration between paralytic episodes of less than two years.

DOCTER, Seattle.

THE SEVERITY OF POLIOMYELITIS IN MULTIPLE-CASE HOUSEHOLDS. CHARLES I. LEFTWICH and JOHN M. CHAPMAN, Pub. Health Rep. **69**:1079 (Nov.) 1954.

In a study of 82 households with multiple cases of poliomyelitis, it has been found that initial cases are more likely to be paralytic than are subsequent cases and that subsequent cases are more likely to be nonparalytic in type as the interval between the initial and the subsequent case increases. Possible interpretations of these results are discussed.

FROM THE AUTHORS' SUMMARY.

DEAFNESS DUE TO RUBELLA. H. O. LANCASTER, M. J. Australia **2**:323-324 (Aug. 28) 1954.

Surveys show that epidemics of rubella are frequently associated with increased incidence of congenital deafness. In areas where rubella is endemic, deafness will appear sporadically rather than in epidemic.

MCGUIGAN, Evanston, Ill.

EARLY AND LATE PULMONARY COMPLICATIONS IN POLIOMYELITIS. TESCOLA FRANCO, Clin. pediat. **36**:459 (June) 1954.

In the early stages of poliomyelitis, atelectasis is the most frequent complication when some of the muscles of respiration are paralyzed; later in the disease, respiratory infections with bronchitis present the more difficult therapeutic problems.

HIGGINS, Boston.

THE LIMITATIONS IN THE USE OF ANTIBIOTIC THERAPY IN DIPHTHERITIC INFECTIONS. A. MURANO, Pediatria **62**:32 (Jan.) 1954.

Although antibiotics may reduce the intensity of the local lesions in patients with diphtheria, the disease may develop malignant characteristics if antitoxin is not also given.

In Naples, the death rate among diphtheria patients has decreased 50% to 70% between the years 1946 and 1953, although the incidence of the disease has been essentially the same in each of the two years.

HIGGINS, Boston.

ERYTHROMYCIN IN EXPERIMENTAL DIPHTHERIA INFECTION IN RABBITS. MICHELE PARADISO and CARMELO LA CAUZA, Riv. clin. pediat. **53**:427 (May) 1954.

The authors treated diphtheria infection in guinea pigs with erythromycin. They conclude that this antibiotic displays a remarkable action against the Corynebacterium diphtheriae and is the more effective the earlier the antibiotic has been administered.

FROM THE AUTHORS' SUMMARY.

ATYPICAL COURSE OF MEASLES AFTER PROPHYLAXIS WITH GAMMA GLOBULIN AND MIXED HUMAN PLASMA. M. BRADACOVA and J. MIROVSKY, Pediat. listy **9**:150, 1954.

An analysis is given of the clinical picture of 44 cases of atypical measles after the prophylactic administration of gamma globulin and mixed human serum. Attention is drawn to the epidemiological importance of the cases in view of the difficult diagnosis and the lasting infectiousness of the mitigated measles.

FROM THE AUTHORS' SUMMARY.

Acute Infectious Diseases

THE C-REACTIVE PROTEIN DETERMINATION AS A MEASURE OF RHEUMATIC ACTIVITY. N. H. SHACKMAN, E. T. HEFFER, and I. G. KROOP, Am. Heart J. **48**:599-611 (Oct.) 1954.

C-reactive protein determinations were performed on the sera of 24 rheumatic fever patients in order to help determine the presence or absence of activity.

There was a close correlation between the inactive state and a negative C-reactive protein determination. However, there were two instances of a negative C-reactive protein in the presence of rheumatic activity.

A positive test in Sydenham's chorea should suggest the presence of an associated carditis.

The C-reactive protein determination was a better guide to activity than the sedimentation rate, which showed protracted elevation despite the inactive state.

FROM THE AUTHORS' SUMMARY.

STAPHYLOCOCCAL INFECTIONS AND THE PROBLEM OF ANTIBIOTIC-RESISTANT STAPHYLOCOCCI. WESLEY W. SPINK, A. M. A. Arch. Int. Med. **94**:167 (Aug.) 1954.

The author reviews the problem of the increasing incidence of antibiotic resistant staphylococci. He discusses at length the various theories as to the mechanisms involved which produce resistant organisms and some of the basic principles related to therapy and advocates that when one is treating any type of staphylococcal sepsis it is essential to pursue an energetic and aggressive treatment with a combination of drugs which have been selected on the basis of sensitivity tests carried out in the laboratory.

JONES, Chicago.

INFECTIOUS DISEASES: NINETEENTH ANNUAL REVIEW OF SIGNIFICANT PUBLICATIONS. HOBART A. REIMANN, A. M. A. Arch. Int. Med. **94**:272 (Aug.) 1954.

This is an extensive review article in which the author summarizes all of the important contributions to the field of infectious disease which were published during the year 1953. There is an extensive bibliography which will be useful to anyone especially interested in this subject.

JONES, Chicago.

THE SURVIVAL OF TRANSFUSED RED CELLS IN ACUTE RHEUMATIC FEVER WITH REFERENCE TO A LATENT HAEMOLYTIC MECHANISM. JOHN REINHOLD, Arch. Dis. Childhood **29**:201 (June) 1954.

The rapidity of the onset of anemia in acute rheumatic fever suggests an underlying hemolytic process.

The survival of transfused red cells has been followed in six control cases and in eight children with acute rheumatic fever. In the control cases disappearance of donor red cells from the recipient's circulation occurred at a steady rate, with a linear slope of elimination. In acute rheumatic fever there was an increased rate of disappearance of donor red cells, with a curvilinear slope of elimination indicating random destruction unrelated to the normal process of aging.

It is concluded that the anemia in acute rheumatic fever is due, at least in part, to a hemolytic process.

KELLY, Milwaukee.

CYTOMEGALIC DISEASE. CASE REPORT. C. NEZELOF and A. ROSSIER, Études neo-natal. **3**:145 (Sept.) 1954.

The authors report a case of cytomegalic disease with congenital icterus.

Postmortem examination showed an acute degenerative hepatitis and cytomegalic inclusions in the liver, the kidneys, the thyroid, the pancreas, and the lungs.

All attempts to inoculate the disease to animals were unsuccessful. It seems, however, likely that the disease is due to a viral infection. The virus is usually present in the salivary glands of 10%-30% of normal newborn infants. It becomes virulent only when the process generalizes in two kinds of circumstances: (1) during extrauterine life, favored then by thrush or administration of antifolic compounds; (2) during intrauterine life, causing, as toxoplasmosis, a fetopathy; at birth, in most of cases, a severe hepatitis ensues, accompanied with diffuse hemorrhages, erythroblastosis, and splenomegaly.

FROM THE AUTHORS' SUMMARY.

PHYSIOLOGIC OBSERVATIONS ON ARTIFICIAL RESPIRATION IN THE TREATMENT OF TETANUS. C. G. ENSTROM, Helvet. paediat. acta **9**:403 (Nov.) 1954.

Artificial respiration in respiratory paralysis, with no special regard as to the genesis, is a substitution therapy in which "too much" as well as "too little" is injurious and is to be avoided. The size of the ventilatory volume is best controlled by means of regularly repeated determinations of the arterial blood gases, especially the CO_2 tension (pCO_2), whereby the job of the disturbed function of the respiratory center is taken over. With this method it is possible to maintain for weeks in optimal fashion the artificial respiration of Curare-treated cases of tetanus. The Engstrom respirator has proved satisfactory in artificial respiration. Our experiences consist of 9 cases of respiratory paralysis of cerebral origin (head injuries and operation), 14 cases of poliomyelitis, and 3 cases of Curare-treated tetanus.

FROM THE AUTHOR'S SUMMARY.

MODERN TREATMENT OF SEVERE TETANUS, E. ROSSI, A. BODMER, M. BETTEX, and K. GRAF, Helvet paediat. acta **9**:425 (Nov.) 1954.

The present view on the treatment of severe tetanus cases is reported. In the first case, "hibernation" plays an important part in recovery. The second case has been treated successfully by the combination of a muscle-relaxing agent (curare) in large doses inducing flaccid paralysis, with artificial respiration (Engstrom respirator) and medicamentous and physical "hibernation." We think that the above-mentioned method might be worth a trial in a severe case.

FROM THE AUTHORS' SUMMARY.

ORAL ADMINISTRATION OF PENICILLIN AS A PROPHYLAXIS IN STREPTOCOCCAL INFECTIONS AT A CHILDREN'S INSTITUTION. SVEN HELBO, Nord. med. **50**:1294 (Sept. 17) 1953.

The author describes the findings in two groups of children, each composed of 70 children, of which one received oral treatment of penicillin, 200,000 units daily, while the other was untreated. At the start of treatment 9 children of the treated group and 10 of the untreated group had streptococci in the nasopharyngeal swab. During treatment samples were taken every second week. There were no streptococcal carriers or streptococcal infections among the treated children, nor were any penicillin-resistant streptococci or complications of the treatment given over a period of nine months observed. Forty-seven days' hospitalization due to cross infections occured in the treated group, 211 in the control group. In the control group 92 samples of streptococci were found and in the controls 20 samples of streptococci were found during treatment. There were 111 days of illness due to Streptococcus infection, as compared to none in the treated group.

WALLGREN, Stockholm.

Chronic Infectious Diseases

THE USE OF SERIAL HEMAGGLUTINATION TESTS IN FOLLOWING THE COURSE OF TUBERCULOSIS IN CHILDREN. VIRGINIA H. PEDEN, KEITH E. VINCENT, and EDITH RICH, Pediatrics **14**:340 (Oct.) 1954.

In cases of known pulmonary (or meningeal) tuberculosis in which x-ray or spinal fluid findings have become stabilized, a rise or fall in a previously stable hemagglutinin titer is a reliable indication that x-ray (or spinal fluid) evidence of improvement of the diseases will follow within a few weeks.

A change in hemagglutinin titer occurring simultaneously with improvement in x-ray (or spinal fluid) findings serves as reliable additional evidence of improvement of the disease.

The significance of a changing hemagglutinin titer must always be evaluated with reference to x-ray (or spinal fluid) findings. A changing titer can be considered evidence of impending or beginning improvement of the disease only if the x-ray (or spinal fluid) findings are either static or improving.

A changing hemagglutinin titer was useful in predicting or confirming improvement of tuberculous disease in 38% of the group of cases studied. In the remaining cases, a change in hemaggluinin titer either failed to occur at all, or did not occur until after definite x-ray (or spinal fluid) improvement had taken place.

The absolute height of the hemagglutinin titer, in itself, was of no prognostic significance in connection with the course of tuberculosis in children.

In following the course of tuberculosis, the hemagglutination test is of more value in older children and in children with relatively mild forms of the diseases than in infants or in patients with severe forms of tuberculosis, because the former are more likely to develop positive tests.

Tuberculin testing did not interfere with the use of the hemagglutination test in following the course of tuberculous disease.

FROM THE AUTHORS' SUMMARY.

ISONIAZID IN THE TREATMENT OF MILIARY TUBERCULOSIS IN CHILDREN. W. P. SWEERNAM and E. F. MURPHY, Arch. Dis. Childhood **29**:338 (Aug.) 1954.

Four children with miliary tuberculosis have been treated with isoniazid alone on a dosage of 10 mg. per kilogram of body weight daily for a year. One case was complicated by tuberculous meningitis and another by tuberculous enteritis. Clinical improvement was rapid, and all remained well after treatment was stopped. Radiological improvement was slow but progressed steadily, the lung fields being clear after 12 months' treatment. No toxic effects were observed.

KELLY, Milwaukee.

INCIDENCE OF CHILDHOOD TUBERCULOSIS WITH PARTICULAR REFERENCE TO PULMONARY TUBERCULOSIS. D. N. SHIVPURI, Indian J. Pediat. **21**:195-204 (Sept.) 1954.

Occurrence of different forms of tuberculosis in children was analyzed in a series of 523 tuberculous children. Twenty-eight per cent of cases had pulmonary tuberculosis. Tuberculous adenitis comprised 90% of the extrapulmonary cases.

In 84 cases of pulmonary tuberculosis, 22.6% had primary tuberculosis. Of the remaining 77.4% with postprimary disease, 47.7% had cavities and 51% were bilateral. About half of the cases producing sputum were positive on smear alone.

In investigating contacts of tuberculosis patients, 52.8% of Mantoux tests were positive. In the 10-15-year age groups, 98% were positive. Of 1008 contacts, 1.2% were found to have pulmonary tuberculosis.

MCGUIGAN, Evanston, Ill.

TUBERCULOSIS OF BONES AND JOINTS. H. R. PASRICHIA, Indian J. Pediat. **21**:218-220 (Sept.) 1954.

The treatment of bone and joint tuberculosis is outlined. In early cases immobilization and antibiotics give good results. In advanced cases, drainage, debridement, extension, and antibiotics are used. Results with this routine have been good.

MCGUIGAN, Evanston, Ill.

THE RESULTS OBTAINED IN THE PEDIATRIC CLINIC OF BOLOGNA WITH THE USE OF SINGLE AND OF VARIOUS COMBINATIONS OF ANTITUBERCULOSIS DRUGS IN THE TREATMENT OF TUBERCULOUS INFECTIONS, ESPECIALLY IN CHILDREN. L. MARTONI and A. DEGLI ESPOSTI, Clin. pediat. **36**:501 (July) 1954.

An analysis is made of the therapeutic results obtained in the treatment of 380 children and 31 adults with lesions of pulmonary tuberculosis and of 214 children and 117 adults with tuberculous meningitis since 1947.

Streptomycin proved to be the most potent drug in exudative lesions, while isoniazid was preferable in localized and hilum gland lesions. However, alternating periods of treatment with streptomycin and isoniazid produced the best clinical results and the quickest recovery in pulmonary lesions.

Also, in tuberculosis meningitis alternate periods of treatment with streptomycin and isoniazid have given the best results; 83% of the patients treated by this combination have been cured, as contrasted to 60% treated by streptomycin alone and 64% by streptomycin and PAS. The percentage of cures in children under 2 years of age (56%) was less than in the older patients (89%).

PAS seemed of value mainly in maintaining the improvement due to the other drugs.

HIGGINS, Boston.

INVESTIGATIONS AS TO THE LOSS OF IMMUNITY BY GUINEA PIGS WHICH HAD BEEN VACCINATED BY BCG. A. DEGLI ESPOSTI, Clin. pediat. **36**:531 (July) 1954.

When guinea pigs had been vaccinated by BCG, it was no longer possible to recover live organisms from their tissues three to four months later. This fact probably explains why the immunity conferred to guinea pigs by BCG is different and less lasting than when virulent tubercle bacilli are used.

HIGGINS, Boston.

THE SIGNIFICANCE OF SPINAL FLUID FINDINGS IN TUBERCULOUS MENINGITIS. P. NICOLAJ, Clin. pediat. **36**:597 (Aug.) 1954.

A study of the constituents of the spinal fluid of patients with tuberculous meningitis furnishes aid both in making a diagnosis and in evaluating therapeutic progress.

The albumin content increases with the severity of the disease or from local irritation from the antibiotics; its highest content occurs in spinal block.

The positive Pandy test is the first abnormal finding to appear and also the last to disappear as the patient gets well.

An increase in the number of white blood cells is also an early finding. Later variations usually are not significant of clinical changes, unless a purulent meningitis is developing.

The glucose content increases with encephalitic involvement but otherwise tends to fall with an increase of the infectious process or as a result of streptomyin therapy.

Variations in the chloride content will parallel those in glucose ordinarily. One exception is in encephalitic episodes, when the chlorides may either fall, rise, or be unchanged. A rapid fall in both glucose and chloride contents may be early indications of a worsening of the clinical picture.

HIGGINS, Boston.

CLINICAL ASPECTS OF NEUROSYPHILIS IN CHILDREN. G. GOMIRATO and M. GOMIRATO-SANDRUCCI, Minerva pediat. **6**:613 (Aug. 31) 1954.

A extensive review of the various types of neurosyphilis in children is accompanied by a report of nine clinical cases. Such cases are notably less frequent at the present time; this is due to the advent of the penicillin therapy for syphilis. While penicillin alone gives better results in neurosyphilis than does the heavy-metal therapy formerly used, a combination of the two has been found to be even better. It is very important to begin treatment of the syphilitic pregnant mother and her syphilitic infant as early as possible.

HIGGINS, Boston.

THE BLOOD AND SPINAL FLUID LEVELS OF THE HYDRAZIDE OF PARAAMINOSALICYLIC ACID FOLLOWING ORAL ADMINISTRATION. F. M. CHIOSSI and M. LINS JR., Minerva pediat. **6**:654 (Aug. 31) 1954.

The giving by mouth of 20 mg. per kilogram of body weight of the hydrazide of para-aminosalicylic acid resulted in a blood concentration of the drug in excess of the minimum amount needed to inhibit the growth of tubercle bacilli in vitro. The drug was found to diffuse readily into the spinal fluid of patients with tuberculous meningitis.

HIGGINS, Boston.

PNEUMOTHORAX IN CHILDREN IN THE LIGHT OF MODERN TUBERCULOSIS THERAPY. WILHELM HEESEN, Med. Klin. **49**:1247 (Aug. 6) 1954.

It is pointed out that on treatment of tuberculosis of the lungs with antibiotics alone recurrences of open tuberculosis occur. With collapse treatment by means of pneumothorax, the results were much better, and it is expected that with additional chemotherapy even better results could be expected. The indications and contraindications for treatment with pneumothorax are discussed, as well as the duration of the treatment.

AMBERG, Rochester, Minn.

SERUM ELECTROPHORETIC STUDIES OF TUBERCULOUS CHILDREN TREATED WITH HIGH DOSES OF ISONIAZID. ROLF HUMBERT, Monatsschr. Kinderh. **102**:432-434 (Oct.) 1954.

Forty children, ranging in ages from early infancy to 15 years, with various forms of tuberculosis were treated for four to six months with isoniazid in the dose of 20 mg/kg/day. Some patients received additional streptomycin and *p*-aminosalicylic acid. Electrophoretic studies

of serum did not reveal any evidence of hepatic damage. Toxic liver changes, either tuberculous or nontuberculous, were not found to be contraindications to this high-dosage regimen of isoniazid.

However, in view of limited experience with this dosage regimen, it should be used only experimentally at the present time.

HARTENSTEIN, Milwaukee.

SPECIFIC (BCG) IMMUNIZATION IN THE TREATMENT OF CHILDREN WITH TUBERCULOUS MENINGITIS. HERBERT GENZ, Monatsschr. Kinderh. **102**:448-450 (Oct.) 1954.

Twenty-five children with tuberculous meningitis received three to five intracutaneous injections of BCG vaccine at 4- to 8-week intervals in addition to streptomycin therapy. Fifteen of these patients survived without tuberculous meningitis three to five years later.

Of 23 children with tuberculous meningitis in a control group who received streptomycin alone, only 5 were alive three to five years later and were considered cured.

HARTENSTEIN, Milwaukee.

THE VALUE OF THE BCG TUBERCULIN FOR THE DIFFERENTIAL DIAGNOSIS BETWEEN ALLERGY AFTER BCG VACCINATION AND AFTER VIRULENT INFECTION. O. RUZICKA, Wien klin. Wchnschr. **66**:759-762 (Oct. 8); 785-789 (Oct. 15) 1954.

BCG tuberculin was prepared much like the old tuberculin from cultures which were used for the preparation of BCG. The problem of the possibility of distinguishing a BCG-induced allergy from one induced by injection with usual tubercle bacilli is discussed at length. It is noted that the sensitivity to tuberculin after BCG vaccination is more readily determined by the use of BCG tuberculin. In cases of illness after BCG vaccination, the simultaneous testing with both kinds of tuberculin permits in the majority of cases a more accurate decision as to whether an allergy due to vaccination or due to injection is present. Patch tests are preferred, and the necessity is stressed of considering the size of the reaction color and infiltration and, when desirable, the duration. BCG tuberculin can show up a vaccination allergy earlier than old tuberculin.

AMBERG, Rochester, Minn.

Diseases of Blood, Heart and Blood Vessels, and Spleen

TREATMENT OF ACUTE LEUKEMIA WITH CORTISONE AND CORTICOTROPIN. PHAEDON FESSAS, M. M. WINTROBE, R. B. THOMPSON, and G. E. CARTWRIGHT, A. M. A. Arch. Int. Med. **94**:384 (Sept.) 1954.

The authors present a short review of the literature and, in addition, present the data on 47 cases of acute leukemia which were treated with hormone therapy. Excellent results were observed in the lymphoblastic variety, complete remissions occurring in 18 out of 22 children (82%) 10 years of age and under and in 3 out of 9 older patients. Partial remissions occurred in another seven cases. There were three failures in this group. In contrast, complete remissions were not observed among 15 cases of acute myeloblastic leukemia, and there were only 2 partial remissions in this group. This form of treatment also failed in one case of acute monocytic leukemia. It was the authors' impression that the leukemic process was accelerated by hormone treatment in some of these cases of myeloblastic and monocytic leukemia. They suggest that hormone therapy should be reserved for the lymphoblastic variety of acute leukemia and that in any other form of acute leukemia such therapy may be contraindicated.

JONES, Chicago.

STURGE-WEBER SYNDROME (ENCEPHALOTRIGEMINAL ANGIOMATOSIS). GERALDINE KING and GABRIEL A. SCHWARZ, A. M. A. Arch. Int. Med. **94**:743 (Nov.) 1954.

The authors present a complete review of the literature dealing with this interesting and rare syndrome, which consists of a vascular nevus of the face, a hemiplegia contralateral to the cutaneous lesion, and intracerebral calcification found roentgenographically ipsilateral to the nevus, various abnormalities of the ipsilateral eyeball, convulsive seizures, and mental retardation. In addition, they give case reports on five patients of their own whose ages when they were first seen ranged from 4 months to 48 years. Only one patient presented all the classic signs and symptoms. The other four had various combinations of the clinical features, the

commonest being the facial nevi, focal seizures, and ocular abnormalities. They point out that the classic signs and symptoms of the Sturge-Weber syndrome may be shuffled considerably from case to case. Three patients were subjected to carotid angiography, and none showed abnormal cerebral vessels or retarded blood flow to the angiomas. Disagreement continues as to proper therapy, although evidence of progression in signs and symptoms has motivated removal of the cerebral lesions, particularly when seizures could not be adequately controlled. The authors feel the more radical surgical approaches are indicated only if proper anticonvulsant therapy has proved a total failure and if the resulting surgical defect would not surpass the patient's presurgical defect. The diagnosis of Sturge-Weber syndrome should be considered in any child who has a vascular nevus of the face.

JONES, Chicago.

DECREASE IN SERUM GAMMA GLOBULIN (AGAMMAGLOBULINEMIA): REPORT OF THREE CASES. ALVIN B. HAYLES, GUNNAR B. STICKLER, and BERNARD F. MCKENZIE, Pediatrics **14**:449 (Nov.) 1954.

A study has been made regarding three boys who had agammaglobulinemia and who were seen at the Mayo Clinic during a period of seven months. In each there was a history of frequent infections since infancy. All three patients demonstrated relatively normal serum proteins except for greatly decreased amounts of gamma globulin. The deficiency in gamma globulin was demonstrated by use of paper electrophoretic analysis of serum proteins.

One of the patients, an infant, died while under treatment at the clinic. The second patient continued to have frequent infections in spite of the administration of gamma globulin at frequent intervals; he died later at home. The third patient has been maintained in good health by monthly injection of gamma globulin.

FROM THE AUTHORS' SUMMARY.

HEMOLYTIC AND PANCYTOPENIC SYNDROME ASSOCIATED WITH LETTERER-SIWE DISEASE. EARLE L. LIPTON, Pediatrics **14**:533 (Nov.) 1954.

Two cases of Letterer-Siwe disease are described in which a hemolytic mechanism was the probable cause of the associated anemia. A review of the pertinent literature indicates that this may be an integral part of the disease in some cases.

The laboratory evidence and clinical response to corticotropin in the first case indicate an extrinsic and probably immunologic mechanism. It is speculated that an analogous process is also responsible for the total pancytopenia. Future acute reticuloendotheliosis cases should be studied in detail in order to elucidate further the etiology of the hematologic changes.

FROM THE AUTHOR'S SUMMARY.

SOME ASPECTS OF THE DYNAMICS OF CONGENITAL HEART DISEASE. GERALD R. GRAHAM, Great Ormond St. J. (No. 7) pp. 1-8, June, 1954.

Diagnosis of congenital heart defects can be assisted by allowing the objective clinical signs to give one evidence of the disturbed dynamics. For example, interference with growth and development is present in interatrial septal defect or one of the cyanotic lesions. Cyanosis since birth indicates a right-and-left shunt with associated overriding aorta or pulmonary stenosis. Slow development of cyanosis indicates a combination of defects leading to a gradual development of right-and-left shunt. X-ray demonstration of chamber enlargement indicates either obstruction to outflow or increased inflow due to a shunt.

MCGUIGAN, Evanston, Ill.

CONGENITAL HEART DISEASE AS SEEN IN COUNTRY PRACTICE. CHARLES RICHARDSON, M. J. Australia **2**:317-318 (Aug. 28) 1954.

A few brief descriptions are given of the commoner cardiac anomalies. The author feels that close attention to diet before and during pregnancy might reduce the number of congenital heart cases seen.

MCGUIGAN, Evanston, Ill.

CONGENITAL CARDIAC CONDITIONS IN THE NEWBORN. KATE CAMPBELL, M. J. Australia **2**:318-320 (Aug. 28) 1954.

Brief diagnostic points are outlined to aid in the diagnosis of congenital cardiac lesions in the newborn period. The author remarks that treatment at this age is largely symptomatic and that the question of prevention must always be a primary concern.

MCGUIGAN, Evanston, Ill.

THE PATTERN OF CONGENITAL HEART DISEASE IN INFANCY AND CHILDHOOD. DOUGLAS STUCKEY, M. J. Australia **2**:433-444 (Sept. 11) 1954.

In one-fifth of the 2- to 13-year group congenital heart disease was of the cyanotic type, and in two-thirds of these the lesion was the tetralogy of Fallot. Of the cyanotic types, patent ductus, septal defects, and pulmonary stenosis accounted for 9 of the 10 cases.

In the 0- to 13-year groups cyanotic forms of the disease were present in almost one-half because of the greater number of cases of transposition, pulmonary atresia, or coarctation of the aorta. Patent ductus was infrequent.

McGUIGAN, Evanston, Ill.

PERIARTERITIS NODOSA IN CHILDHOOD. F. SCHMID and A. WEISS, Monatsschr. Kinderh. **102**:442-448 (Oct.) 1954.

One hundred eight cases of periarteritis nodosa in childhood have been reported in the world literature. The authors add another case, that of a 3-year-old girl who developed periarteritis nodosa in the course of a fulminating, nontypical miliary tuberculosis and died three weeks after onset of her illness.

Review of the literature showed no sex predilection as in adults. Heart, kidney, liver, spleen, and gastrointestinal tract were the organs most commonly involved. The most frequent clinical manifestations were fever, generalized body pains, edema, weight loss, neuritis, dyspnea, leucocytosis, proteinuria, and hematuria. Duration of the disease varied from hours to years. Of all reported cases of periarteritis nodosa, 10% to 15% were in children. It is a hyperergic reaction of small blood vessels. Streptococcic focal infection probably is the most important etiologic factor, although many theories have been advanced. Combination of cortisone and antibiotics offers the most hope in the treatment of this disease.

HARTENSTEIN, Milwaukee.

RARE BLOOD GROUPS. J. J. VAN LOGHEM JR., MIA VAN DER HART, and HELENE BOSMAN, Maandschr. kindergeneesk. **22**:357 (Nov.) 1954.

The authors describe two new rare blood-group antigens, which have provisionally been designated as Vw and Rm.

The corresponding antibodies were the result of isoimmunization during pregnancy.

As far as could be ascertained by investigation, the new antigens were not identical with other, previously reported, so-called "private" or "familial" antigens.

The heredity of the two blood groups was established by demonstrating the presence of the antigen in six members of two generations and in six members of three generations, respectively.

The factor Vw is probably linked to the MNSs system.

FROM THE AUTHORS' SUMMARY.

Diseases of Nose, Throat, and Ear

THE DEVELOPMENT AND EVALUATION OF A SPEECH IMPROVEMENT PROGRAM FOR KINDERGARTEN CHILDREN. BETTY ANN WILSON, J. Speech & Hearing Disorders **19**:4-13 (March) 1954.

One hundred twenty-eight experimental subjects in a 12-week speech improvement program for kindergarten children versus one hundred fourteen controls were studied by means of checking p, b, m, n, t, d, k, g, f, l, r, s before and after the 12-week period. There was a significant reduction in the mean number of articulation errors made on sounds included in the speech-improvement lessons. Six additional sounds not included in the program were also tested before and after the 12-week study, with reduction in numbers of errors. Reading readiness scores did not significantly change on the basis of the work done.

PALMER, Wichita, Kan.

SYSTEMATIC RESEARCH IN EXPERIMENTAL PHONETICS: THE EVALUATION OF SPEECH SIGNALS. GORDON E. PETERSON, J. Speech & Hearing Disorders **19**:158-168 (June) 1954.

The constructs of linguistic theory pose a major challenge to those who would study speech processes. Is it possible to find within the central nervous system activities which correspond

in their occurrences to the occurrences of phoneme and morpheme reception during the actual listening process? High intelligibility for certain prolonged synthetic vowels and very short vowels indicates structuring importance of the higher formants on vowel specificity.

PALMER, Wichita, Kan.

THE ROLE OF THE OTOLARYNGOLOGIST IN THE MANAGEMENT OF ACUTE LARYNGOTRACHEITIS. BLAIR FEARON, Canad. M. A. J. **71**:482-484 (Nov.) 1954.

The author presents a concise discussion of the problem of laryngotracheitis, with a plea for more frequent use of tracheotomy in the management of this disease.

McGUIGAN, Evanston, Ill.

NON-INFLAMMATORY LARYNGEAL STRIDOR IN INFANTS. JAMES CROOKS, Arch. Dis. Childhood **29**:12 (Feb.) 1954.

"Congenital laryngeal stridor" is a clinical description and should not be used to denote the specific entity of inspiratory laryngeal collapse of infants. This condition is described and also another developmental abnormality the baby outgrows, which the writer calls inspiratory arytenoid prolapse.

Case records are given of eight babies with laryngeal stridor due to localized conditions in the larynx, open to surgical treatment and if not so treated likely to prove fatal. Four of the babies had cysts, two hemangiomas, one a cleft larynx, and one a foreign body.

The larynx of a baby with stridor should be inspected to establish the cause.

The difficulties and dangers of tracheostomy in young infants are discussed.

KELLY, Milwaukee.

MYOBLASTOMA OF THE LARYNX. I. P. J. MACNAUGHTAN and M. S. FRASER, J. Laryng. & Otol. **68**:680 (Oct.) 1954.

An extensive sessile tumour on the posterior wall of the larynx caused hoarseness and stridor in a boy aged 9 years. It was recognized as a granular-cell myoblastoma and is the first example to be reported in the larynx of a child. The growth was excised by laryngofissure but recurred seven months later. Radiotherapy was unsuccessful, and laryngectomy was ultimately required. Analysis of previous reports of laryngeal myoblastoma, with reference to clinical features and treatment, shows that this was an exceptionally severe case.

FROM THE AUTHORS' SUMMARY.

THE EARLY RECOGNITION OF DEAFNESS IN CHILDHOOD. V. L. COLLINS, M. J. Australia **2**:324-328 (Aug. 28) 1954.

Emphasis is placed on the earliest possible recognition of deafness, so that speech training and hearing aids may be used early. The most appropriate time is in the second year of life.

McGUIGAN, Evanston, Ill.

PROBLEMS OF THE DEAF CHILD AND INCIDENCE AND INSTITUTIONS. F. W. CLEMENTS, M. J. Australia **2**:328-329 (Aug. 28) 1954.

Better facilities are needed to detect children with hearing loss in order that they may be treated before impairment becomes severer. Schooling depends on the degree of loss.

Children with a loss of 30 to 65 db., after being fitted with a hearing aid, can frequently be placed in normal schools. With a loss of 65-85 db., some children can attend regular schools using a hearing aid or can attend special acoustic schools; these children can live normal lives. With a loss of 85 db. or more, lipreading is required and the opportunity to lead a normal life is limited.

McGUIGAN, Evanston, Ill.

SPUTUM SMEARS AS A SOURCE OF AN INFECTIOUS AEROSOL. F. DEKKING, Nederl. tijdschr. geneesk. **98**:1626 (June) 1954.

Most laboratory infections are due to ignorance and indifference of laboratory workers. By careful working many infections can be prevented. Some techniques, however, offer a constant

danger to those using them. Some of these techniques are mentioned. Dekking demonstrated by means of electronic flash photographs that a common technique of making sputum smears between two slides may be the source of an infectious aerosol.

VAN CREVELD, Amsterdam.

Diseases of Lungs, Pleura, and Mediastinum

COMPARATIVE RESULTS OF THE USE OF ACTH, CORTISONE, AND HYDROCORTISONE IN THE TREATMENT OF INTRACTABLE BRONCHIAL ASTHMA AND PULMONARY EMPHYSEMA. HYLAN A. BICKERMAN, and ALVAN L. BARACH, J. Allergy **25**:312 (July) 1954.

Corticotropin (ACTH), cortisone, hydrocortisone, or a combination, were used on a group of 107 patients with intractable asthma and 56 patients with severe pulmonary emphysema. There were 89 men and 74 women, ranging in age from 11 to 78 years.

All patients were placed on a low-sodium diet and received 1 gm. of enteric-coated potassium chloride three times a day.

Complete or partial remission occurred in 82.3% of the patients who had received corticotropin, in 86.2% of those who received cortisone, and in 96% of those who received hydrocortisone at a dosage level 50%-60% of that employed with cortisone.

The effects produced by hydrocortisone differed from those produced by cortisone. With the former, the effect was produced more rapidly with a smaller dose and with fewer side-reactions.

HOYER, Cincinnati.

IDIOPATHIC PULMONARY HEMOSIDEROSIS. F. G. FLEISCHNER and A. L. BERENBERG, Radiology **62**:522-526, 1954.

The diagnosis of hemosiderosis was corroborated by the demonstration of iron pigment in a biopsy specimen obtained by lung puncture in a Negro boy 2 years of age. The roentgen findings consisted of symmetrical homogeneous opacities, densest in the central portion of the lung. The patient was observed for a period of seven months, with replacement of the haziness in the lung field by a more nodular pattern of consolidation in a field of almost normal radiance. The patient was well more than two years later. A low-grade fever and severe anemia were the most constant clinical manifestations during the period of active observation. The absence of notable respiratory infection combined with hypochromic anemia without a generalized hemolytic tendency coupled with the x-ray findings should suggest idiopathic pulmonary hemosiderosis. The demonstration of hemosiderin in the sputum, gastric washings, or lung tissue obtained by biopsy should establish the diagnosis.

The rarity of the diagnosis of pulmonary hemosiderosis is illustrated by this condition being reported only four times in the American literature.

[Abstractor's Comment.—The author states that this reviewer made the first roentgenologic observation (1939). I might add that since my report included the clinical and pathological observations, it predated Waldenstrom (1944), who, the author states, was the first to correlate the x-ray, clinical, and pathological aspects, by five years.]

ANSPACH, Riverside, Ill.

TENSION EMPHYSEMA: A SURGICAL EMERGENCY IN INFANTS. Y. T. NELSON and DOUGLAS REYE, M. J. Australia **2**:342-343 (Aug. 28) 1954.

Four cases of tension emphysema are reported, with two fatalities. Two were cured by lobectomy, and the other two died, having been seen as emergency cases. The cause was considered to be absence of bronchial cartilage in the bronchus of the affected lobe. Prompt surgical intervention is required in these cases.

MCGUIGAN, Evanston, Ill.

THE TREATMENT OF SPASTIC BRONCHITIS IN CHILDREN WITH KHELLIN. FRIEDRICH WERMINGHAUS, Monatsschr. Kinderh. **102**:450-451 (Oct.) 1954.

Forty-four children with spastic and asthmatic bronchitis were treated with Khellin. Of these, 25 received the drug orally, 15 per rectal suppositories, and 5 intravenously. Dosage was 7-10 mg/kg/day. Average duration of treatment was seven days. No untoward side-effects attributable to Khellin were observed. The drug took effect rapidly and was considered beneficial

in 36 cases (81.7%). Seven children obtained some degee of relief, and one patient was not benefited. Results were less dramatic in children with true bronchial asthma than in those without the classical form of the disease.

HARTENSTEIN, Milwaukee.

THE SIGNIFICANCE OF BRONCHOSCOPY IN SUPPURATIVE PULMONARY DISEASE OF CHILDREN AND INFANTS. L. SABATA and H. VENCLIK, Pediat. listy **9**:143, 1954.

An account is given of the endoscopic treatment of 12 children and infants with pulmonary abscess and of 5 with bronchiectasis. The importance is stressed of removing the bronchial obstruction along with thorough parenteral treatment.

FROM THE AUTHORS' SUMMARY.

Diseases of Gastrointestinal Tract, Liver, and Peritoneum

CONGENITAL CAPILLARY HEMANGIOMA OF THE PAROTID SALIVARY GLAND. ALFRED EDWARDS, MARTIN SWERDLOW, and LORENZO BERRY, A. M. A. Arch. Otolaryng. **60**:615 (Nov.) 1954.

A case of a congenital capillary hemangioma of the right parotid salivary gland in a 16-month-old white girl is presented. These hemangiomata are usually removed surgically with or without preservation of the facial nerve. They are nonmalignant.

KIMBALL, Evanston, Ill.

TRACHEO-ESOPHAGEAL FISTULA WITHOUT ATRESIA. GEORGE WILLIAM WARE and LOUIS L. CROSS, Pediatrics **14**:254 (Sept.) 1954.

Congenital tracheoesophageal fistula without atresia of the esophagus is a rare anomaly. Twenty-six patients are reported in the literature. The authors report an additional case. The etiology is still obscure, but may be due to the development of aberrant blood vessels.

Patients present a triad of signs and symptoms, coughing and cyanosis with feedings, abnormal distention of gastrointestinal tract, and persistent pneumonitis.

Radiographic investigation is most important. Iodized oil (Lipiodol) study of the esophagus in the oblique or prone position is the most rewarding diagnostic test.

Surgery is the only method of cure.

FROM THE AUTHORS' SUMMARY.

VENO-OCCLUSIVE DISEASE OF THE LIVER. DERRICK B. JELLIFFE, GERRIT BRAS, and KENNETH L. STUART, Pediatrics **14**:334 (Oct.) 1954.

The clinical picture and autopsy findings of a fatal case of veno-occlusive disease of the liver (V. O. D.) occuring in a 10-month-old Jamaican infant is reported. Points of similarity between V. O. D. and Budd-Chiari's syndrome, Senecio poisoning, and Indian infantile cirrhosis are noted. The possibile etiology of V. O. D. is considered. It is postulated that V. O. D. is an important cause of cirrhosis of the liver in Jamaican children.

FROM THE AUTHORS' SUMMARY.

THE EFFECT OF CHLORAMPHENICOL IN SALMONELLA ENTERITIS OF INFANCY. W. B. MACDONALD, FREDA FRIDAY, and MERRAN MCEACHARN, Arch. Dis. Childhood **29**:238 (June) 1954.

Fifty-one infants less than 2 years old suffering from Salmonella enteritis were subjected to a controlled therapeutic trial to test the efficacy of chloramphenicol in the disease.

Forty-eight of the infants were infected by S. typhimurium.

Chloramphenicol at a dose of 120 mg/kg/day had no effect in influencing the rate of clinical recovery.

Despite a high degree of sensitivity to chloramphenicol in vitro, the growth of Salmonella in the bowel was not significantly affected by the drug.

KELLY, Milwaukee.

INTESTINAL OBSTRUCTION AS A LATE COMPLICATION OF FIBROCYSTIC DISEASE OF THE PANCREAS (MUCOSIS). O. D. FISHER, Arch. Dis. Childhood **29**:262 (June) 1954.

A case of intestinal obstruction due to inspissated small-bowel contents at 15 months of age is reported. Occurring as a late complication of fibrocystic disease of the pancreas, the similarity to meconium ileus is discussed. Attention is drawn to the condition, which is best treated by ileostomy and pancreatin therapy.

KELLY, Milwaukee.

ANOMALIES OF THE VITELLO-INTESTINAL DUCT. DOUGLAS H. COHEN, M. J. Australia **2**:173-178 (July 31) 1954.

The history of the discovery of Meckel's diverticulum and the embryology of the vitello-intestinal duct are reviewed. Anomalies due to persistence of part or all of the duct are listed and discussed, including a detailed discussion of the problem of Meckel's diverticulum.

McGUIGAN, Evanston, Ill.

APPENDICEAL COLIC. ROBERT SOUTHBY, M. J. Australia **2**:344-345 (Aug. 28) 1954.

The author presents four cases of vague recurrent abdominal pain which were cured by appendectomy. In all the appendix either failed to visualize with barium or failed to fill completely, and in each case the operation revealed kinking, fecoliths, or occlusion of the lumen of the appendix.

McGUIGAN, Evanston, Ill.

RETRO-COSTO-XYPHOID DIAPHRAGMATIC HERNIAE. ROGER EVEN, CHRISTIAN SORS, and RENE CODIS, Presse méd., Supp. 63, p. 1302, Sept. 29, 1954.

Retrocostoxyphoid herniae show an incidence of 3% to 5% in the whole of diaphragmatic herniae; they issue through Larcy's fissure or its close vicinity and almost always on the right side when spontaneous. They are seen at any age and more frequently in men than in women. They appear in a simple or mixed form, the latter being gastrointestinal, epiplointestinal, or varying.

They are or are not accompanied with functional manifestations either digestive or respiratory or both. They are radiologically shown by a hemithoracic image, clear or opaque, or both, low-situated and varying according to the moment.

Except for the latent forms that are casually discovered by x-rays, they are clinically and radiologically demonstrated as follows: the gastric and intestinal forms, by digestive disorders and hyperclarities; the epiploic and hepatic forms, by respiratory disorders, opacities; the mixed forms, by digestive and respiratory disorders, opacities, hyperclarities.

They should be distinguished from pleuropericardial cysts and diaphragmatic deformities, such a discrimination being radiologically facilitated by gastrocolic barium saturation and pneumoperitoneum. Radical surgical cure is advisable, even for the epiploic forms, as they are liable to strangulation or may conceal a gastrointestinal form.

Only for hepatic herniae is surgical abstention preferable.

FROM THE AUTHORS' SUMMARY.

REACTIONS OF HANGER AND OF MACLAGAN IN HEPATIC DISEASES IN THE INFANT. LUIGI CAPOTORTI, Arch. ital. pediat. e puericolt. **16**:484, 1954.

After having explained the peculiarities of the hepatic pathology in children, the author emphasizes the importance of the laboratory for the differential diagnosis and for the prognosis of these diseases. The author studied the meaning and value of the tests of colloidal instability, particularly of two among them which are now the most used, the Hanger cephalin-cholesterol test and the Maclagan thymol turbidity test.

On the basis of an investigation of the chemical mechanism of each of them and of the statistics provided by literature, the author concluded that these two tests, though they cannot be considered closely specific for hepatic diseases, are in such diseases a well-founded indication, either for the generic diagnosis of hepatic damage or for the differentiation of obstructive from hepatocellular jaundice.

Being acquainted with the different mechanism of these two tests, a greater diagnostic information is given by using them both.

FROM THE AUTHOR'S SUMMARY.

EOSINOPHILIA IN TOXICOSIS IN THE INFANT. ALFREDO U. RAMON GUERRA, NELLY TEMESIO, and IBERIA GARCIA ZORRON, Arch. pediat. Uruguay **25**:517 (Aug.) 1954.

During the period of plenary toxicosis (anhydremia, exsicaosis), we observed as a rule, an extreme eosinopenia, generally or very near zero. This fact has been determined by excluding all other factors of important eosinopenia, with restriction to the cases not yet treated. All the

cases which presented convulsions (very common in toxicosis) were excluded, the extraordinary eosinopenic effect of the convulsions having been already demonstrated.

By the time the child is coming out of the state of toxicosis, the number of eosinophiles increases quite rapidly, and generally comes to normal levels toward the end of the first week of treatment. Extreme eosinopenia lasts a much shorter time, since generally on the third day the child has come out of these extremely low values, passing to a moderate eosinopenia.

In lethal cases of toxicosis, the numbers have remained very low till death (seven cases in this new series).

In cases in which no frank orthodox response to the treatment had been obtained, the figures remained low, or did not rise in the expected regular way, but rather maintained the eosinopenia, being a sign of reserved prognosis.

In diarrheic cases which do not reach the state of toxicosis, the values do not as a general rule come to this extreme point, and by this we can establish a relationship between eosinopenia and toxicosis.

FROM THE AUTHORS' SUMMARY.

ON THE QUESTION OF CONGENITAL MICROCOLON. KAREL BARTA, Pediat. listy **9**:240, 1954.

A case of congenital microcolon in a 7-week-old boy is described, with typical clinical features. The relationship of meconium ileus to the origin of this anomaly is discussed. The author does not regard congenital microcolon as a separate clinical entity and rejects the term microcolon as unfitting. He proposes for this anomaly the term stenocolon instead.

FROM THE AUTHOR'S SUMMARY.

Nervous Diseases

THE ATHETOID SYNDROME IN CEREBRAL PALSY: PART II. CLINICAL ASPECTS. LEO J. KOVEN and STANLEY S. LAMM, Pediatrics **14**:181 (Sept.) 1954.

The authors have attempted to illustrate some of the principal clinical aspects of the athetoid syndrome. The universal characteristics, clinical varieties, and other clinical features, as well as the reflex, functional, and orthopedic alterations of these patients, are discussed.

FROM THE AUTHORS' SUMMARY.

CEREBROSPINAL FLUID STUDIES IN INFANT CHILDREN WITH CEREBRAL PALSY AND OTHER NEUROLOGIC DISORDERS. M. SPIEGEL-ADOLF, H. W. BAIRD III, E. G. SZEKELY, and H. T. WYCIS, Pediatrics **14**:215 (Sept.) 1954.

In 100 children with cerebral palsies and various types of developmental cerebral disorders and 32 neurologically normal controls, the extinction coefficient of the C. S. F.'s ($E_{C.S.F.}$) was studied by spectrography in ultraviolet light, and their ascorbic acid and protein contents were determined. From these determinations, the extinction coefficients corresponding to the scorbic acid ($E_{Asc.}$) and protein values ($E_{Prot.}$) and the difference, $D = E_{C.S.F.} - E_{Asc.} - E_{Prot.}$, were computed.

Normal newborn infants presented much higher values of $E_{C.S.F.}$, ascorbic acid, and proteins than older children.

A marked increase of the average D values was noticeable in the neuropathologic group, which included cases of birth trauma, cerebral palsy, mental retardation, hydrocephalus, and convulsions. The increase of D values when statistically evaluated and compared with the analogous values of children without neurological conditions was significant in all pathologic groups (with trauma, mental retardation cerebral palsy, hydrocephalus) with the exception of convulsions.

Mental deficiency, especially in its severe forms, is associated with changes in the C. S. F. indicative of damage to cells of the C. N. S. A correlation is noted between the developmental quotient and the D values; higher D values were found in the group with DG's below 50%, than in that with DQ's above 50%.

Changes of D appearing on repeated punctures could be correlated to the clinical course of the disease; this special problem, however, requires further studies on a larger material.

FROM THE AUTHORS' SUMMARY.

INFANTILE SPASTIC HEMIPLEGIA: I. INCIDENCE. MEYER A. PERLSTEIN and PHILIP N. HOOD, Pediatrics **14**:436 (Nov.) 1954.

The following facts seems to emerge concerning the nature and clinical correlations of various factors in the infantile spastic hemiplegic population.

The mean age for this series at the time of first examination was 6.5 years; means are consistent between large groupings where comparisons were made.

There were more right than left spastic hemiplegics (5:4).

Spastic hemiplegia occurred more often in males than in females (5:4).

The Negro subjects were distributed fairly randomly through the present spastic hemiplegic population; the nonsignificant differences in distribution which occurred were thought to be related to geographical and socioeconomic factors and not to race, per se.

The incidence of postnatally acquired cases was approximately one-third of the spastic hemiplegic series, as compared to one-tenth of the total cerebral palsied population.

The incidence of convulsions in this series was significantly higher than that reported for the general population, for all types of brain injury, for mixed spastic groups, and for most other series of spastic hemiplegics.

Congenital and postnatally acquired cases, convulsive and nonconvulsive cases, and males and females were all distributed randomly between the left and right spastic hemiplegics of this series.

Congenital and postnatally acquired cases, as well as convulsive and nonconvulsive cases, were distributed at random between the males and females of this series.

The postnatally acquired cases of spastic hemiplegia showed a significantly greater incidence of convulsions than the congenital group.

FROM THE AUTHORS' SUMMARY.

A NEW SYNDROME: PROGRESSIVE FAMILIAL INFANTILE CEREBRAL DYSFUNCTION ASSOCIATED WITH AN UNUSUAL URINARY SUBSTANCE. JOHN H. MENKES, PETER L. HURST, and JOHN M. CRAIG, Pediatrics **14**:462 (Nov.) 1954.

Four cases of a syndrome involving a rapidly progressive cerebral dysfunction and commencing during the first week of life are reported. In each of these cases the urine excreted had a peculiar odor, resembling that of maple syrup. The pathogenesis of this condition is unexplained, although some anomaly of cerebral metabolism seems to be the most likely cause of the syndrome.

FROM THE AUTHORS' SUMMARY.

ACUTE SUBDURAL HEMORRHAGE AT BIRTH. RAYMOND SCHIPKE, DAVID RIEGE, and WILLIAM B. SCOVILLE, Pediatrics **14**:468 (Nov.) 1954.

The term "acute subdural hemorrhage of the newborn" has been suggested for comparison with subarachnoid hemorrhage of the newborn and chronic subdural hematoma of infancy.

Two cases of subdural hemorrhage in the newborn, treated by subdural drainage, are presented in detail. Five additional cases discovered at autopsy are discussed.

Increased tension of the fontanelle is the most important single sign for directing attention to the possibility of subdural bleeding at birth.

Early recognition as a prerequisite for favorable therapy is emphasized. Subdural bleeding of clinical significance is best demonstrated by coronal subdural taps.

FROM THE AUTHORS' SUMMARY.

A CASE OF MEDULLOBLASTOMA IN A CHILD AGED EIGHT AND ONE-HALF MONTHS. THEODOR ZONDEK, Ann. pædiat. **183**:218 (Oct.) 1954.

A case of medulloblastoma in a child, aged 8½ months, is described in which the tumor blocked the outflow of the C. S. F. from the aqueduct, therefore causing internal hydrocephalus. There were also some associated congenital abnormalities.

FROM THE AUTHOR'S SUMMARY.

AIMED COMPLEX THERAPY OF CENTRALLY CONDITIONED DISORDERS OF SPEECH IN CHILDREN. E. PAKESCH and F. DOUBEK, Schweiz. med Wchnschr. **84**:950 (Aug. 14) 1954.

In certain cases of disorders of speech associated with disorders of the cerebrum, treatment with large doses of glutamic acid combined with Anirrit was instituted in addition to speech therapy and therapeutic pedagogic measures. Anirrit is a bromide hydantoin compound with a

small amount of phenyl ethyl barbituric acid, which diminished the restlessness and irritability of feeble-minded children due to large doses of glutamic acid. The best results were obtained when the therapy was started at nursery school age. An improvement of speech and of intelligence could be obtained sufficient for admission to school. For further detail the paper is to be consulted.

AMBERG, Rochester, Minn.

Psychology and Psychiatry

PSYCHODYNAMIC CONCEPTIONS IN CHILDREN WITH CHRONIC CEREBRAL LESIONS. G. MORA, Minerva pediat. **6**:14 (Jan. 15) 1954.

The child with an acquired brain injury will present a different behavior pattern from the child who was congenitally deficient. His attitude has many characteristics similar to adults who have suffered from a brain injury. His sensory perception will have been changed and form a basis for his changed personality, especially for his anxiety and the disorganization of his ego functions. Such parental influence as repression, overprotection, and rejection will definitely affect the child's emotional development and behavior.

HIGGINS, Boston.

OBSERVATIONS ON THE SKELETAL AGE IN MONGOLISM. P. MENGHI, Minerva pediat. **6**:81 (Feb. 15) 1954.

Sixteen children, 3 to 13 years of age, each a Mongolian idiot, were evaluated as to their skeletal age from x-ray films and as to their deviation from normal weight and height for their individual ages. The statural age exceeded the chronological age by over 6 months in only 2 of the children; it was 6 months or more less than the chronological age in 10 of the children. Similarly the weight age was higher than the chronological age in 3 children and lower in 9 children, while the skeletal age was higher in 1 child and lower in 12 children. The deviations from normal were more marked in the girls than in the boys. These deviations do not seem to be due to fundamental changes in the order or the nature of the ossification of the bones.

HIGGINS, Boston.

THE COMBINATION OF MONGOLOID HABITUS AND CONGENITAL MALFORMATIONS OF THE HEART. RUDOLF HAMBACH, Ann. pædiat. **183**:77 (Aug.) 1954.

During the course of 21 months the author observed 34 cases of congenital malformation of the heart and of the main vessels. The findings in both groups are shown in tables. Contrary to others, the author frequently saw transposition of the vessels in Mongoloid idiots, besides the changes commoner in Mongolism, such as atrial defects and persisting atrioventricular ostium. The author suspects a hypothetical damaging agent which affects the fetus at the time when the torsions and countertorsions of the truncus septum occur is responsible for the combination of Mongolism and malformation of the heart.

FROM THE AUTHOR'S SUMMARY.

Diseases of Ductless Glands; Endocrinology

COEXISTING DIABETES MELLITUS AND ADDISON'S DISEASE. EUGENE R. STANTON, H. WALTER JONES JR., and ALEXANDER MARBLE, A. M. A. Arch. Int. Med. **93**:911 (June) 1954.

The authors briefly review the literature concerning the coexistence of diabetes mellitus and Addison's disease. This combination is a rarity, and they found only 45 cases reported. The authors give case reports on two additional patients, in one of which the diagnosis of diabetes mellitus was made at the age of 2½ years and the diagnosis of Addison's disease was made at the age of 10. It is stressed that recognition of this combination is important, since, with modern therapy, both conditions can be successfully treated and useful life made possible. Addison's disease, developing in a diabetic, is characterized by diminution in insulin requirements with frequent hypoglycemic reactions.

JONES, Chicago.

METABOLIC COMPETITION BETWEEN DESOXYCORTICOSERONE ACETATE AND STROPHANTHIN-G IN THE RAT. LYTT I. GARDNER, HELEN BERMAN, and HELEN WENDLER DEAN, Endocrinology **55**:417-425 (Oct.) 1954.

Since there is a degree of structural similarity between the cardiac aglucones and the sodium-retaining steroids of the adrenal cortex, there are theoretical grounds for the existence of a

metabolic competition. Experimental data bearing on such a possible relationship are desirable for elucidation of the mechanism of action of the cardiac glycosides.

The results suggest that a metabolic antagonism exists between desoxycorticosterone acetate and ouabain in the rat. JACOBSEN, Buffalo.

HYPERGLYCEMIC AND GLYCOGENOLYTIC ACTIVITY OF PREPARATIONS FROM HUMAN URINE. F. MOYA and M. M. HOFFMAN, Endocrinology **55**:439-447 (Oct.) 1954.

A crude concentrate or an alcohol-insoluble fraction derived from the urine of normal men and women has consistently been found to be hyperglycemic and to induce an increased release of glucose by rabbit-liver slices in vitro. Unlike pancreatic glucagon, the urinary factor is very active in stimulating glycogen breakdown in liver homogenates. JACOBSEN, Buffalo.

FURTHER STUDIES ON THE EFFECTS OF ADRENAL MEDULLARY HORMONES ON RENAL EXCRETION OF WATER AND ELECTROLYTES IN THE INTACT RAT. FREDERIC A. GIERE, Endocrinology **55**:448-455 (Oct.) 1954.

The data presented here favor the view that the adrenal medullary hormones have a qualitatively similar action, but differ quantitatively, in enhancing water, sodium, and chloride output and potassium retention during water diuresis in the rat. JACOBSEN, Buffalo.

THE EFFECT OF GROWTH HORMONE ON MUSCLE POTASSIUM AND ON EXTRACELLULAR FLUID. ADRIENNE A. BATTS, LESLIE L. BENNETT, JOSEPH GARCIA, and JEROME STEIN, Endocrinology **55**:456-465 (Oct.) 1954.

It is concluded that growth hormone (GH) causes an expansion of the extracellular fluid space, which explains the previously observed Na and Cl retention. Also, GH plays some role in maintaining the muscle K. JACOBSEN, Buffalo.

A COMPARISON OF THE ANEMIA PRODUCED BY HYPOPHYSECTOMY WITH THAT RESULTING FROM COMBINED THYROIDECTOMY, ADRENALECTOMY AND GONADECTOMY. A. N. CONTOPOULOS, M. E. SIMPSON, D. C. VAN DYKE, J. H. LAWRENCE, and H. M. EVANS, Endocrinology **55**:509-515 (Oct.) 1954.

Evidence has been presented that the pituitary contains an erythropoietic factor which stimulates red blood cell formation in the rat. The erythropoietic factor has not been identified with any of the known pituitary hormones, and it appears to be a distinct substance.

In experiments here reported, thyroidectomized, adrenalectomized, orchidectomized male rats developed a moderate anemia as compared to the severe and progressive anemia of the hypophysectomized rat. These observations are interpreted as strengthening the hypothesis that the pituitary produces an erythropoietic factor necessary for normal erythropoiesis.

JACOBSEN, Buffalo.

IRRADIATION AND ADRENAL STEROIDOGENESIS: STEROID TRANSFORMATIONS BY IRRADIATED ISOLATED PERFUSED CALF ADRENALS. GEORGE ROSENFELD, FRANK UNGAR, RALPH I. DORFMAN, and GREGORY PINCUS, Endocrinology **56**:24-29 (Jan.) 1955.

The main objective of these investigations was the study of steroidogenic function in perfused adrenals, isolated from the metabolic influences of other tissues and exposed in vitro to gamma radiation in order to investigate the primary effects of ionizing radiation on corticosteroidogenic enzymatic systems.

The present studies corroborate the view that the adrenal cortex is a radioresponsive tissue functionally and indicate that the effect of an ionizing radiation is exerted on all the steroidogenic enzyme systems of the biosynthetic mechanism. JACOBSEN, Buffalo.

IRRADIATION AND ADRENAL STEROIDOGENESIS: INFLUENCE OF IRRADIATION OF ISOLATED ACTH-STIMULATED CALF ADRENALS ON THEIR CORTICAL OUTPUT. FRANK UNGAR, GEORGE ROSENFELD, RALPH I. DORFMAN, and GREGORY PINCUS, Endocrinology **56**:30-36 (Jan.) 1955.

Exposure of the isolated corticotropin-stimulated calf adrenal to moderate doses of gamma radiation (Co^{60}) during perfusion resulted in a significantly decreased secretion of hydrocortisone, corticosterone, and unidentified Porter-Silber chromogens. JACOBSEN, Buffalo.

THE METABOLISM OF THYROTROPHIC HORMONE IN THE RAT. SAVINO A. D'ANGELO, Endocrinology **56**:37-45 (Jan.) 1955.

The precise mode of action of TSH on the thyroid cell is unknown. There is much uncertainty also regarding the locus of degradation and metabolic fate of this trophic principle in the organism.

The concept is offered that the removal of thyrotrophin from the blood is primarily influenced by metabolic levels in tissues responsive to the thyroid hormone.

JACOBSEN, Buffalo.

CONGENITAL GOITER IN A NEWBORN INFANT, DUE TO ANTITHYROID DRUG ADMINISTERED TO THE MOTHER DURING PREGNANCY. P. MARUSSI-SCARIZZA, Minerva pediat. **6**:433 (June 30) 1954.

A newborn baby boy had a very large goiter, involving the entire thyroid gland. There were evident signs of hypothyroidism—lassitude and macroglossia.

The mother had been given methyl-thiouracil (0.1 gm. daily) for hyperthyroidism throughout her pregnancy. During this period, the signs of hyperthyroidism had increased, and her basal metabolism had risen to +78; while in labor she had dyspnea and a sense of suffocation. After the birth of the child, the medication was stopped; her basal metabolism fell to +18, and the signs of hyperthyroidism regressed.

The baby received no therapy. The goiter rapidly decreased in size, and the signs of hypothyroidism disappeared, so that when one month of age, the infant appeared normal.

There appears to be danger in treating a pregnant mother with hyperthyroidism by means of the antithyroid drugs.

HIGGINS, Boston.

RETARDED GROWTH AND GONADAL INSUFFICIENCY. JAKOB ØSTER, Acta pædiat. **43**:318 (July) 1954.

Two cases are reported of Turner's syndrome in female patients. In addition, an account is given of a boy whose symptomatology highly suggests that he belongs pathogentically to the same group. It is emphasized that therapeutic substitution therapy is definitely indicated in the cases of girls, though the pathogenesis is obscure. Further, it is pointed out that attention should be focused on testicular insufficiency in boys with a suspected Turner's syndrome and that substitution therapy should be tried here, too.

FROM THE AUTHOR'S SUMMARY.

Diseases of Muscles, Bones, Joints, and Lymph Nodes

PARAMYOTONIA. WILLIAM TSCHUMY JR., A. M. A. Arch. Int. Med. **94**:443 (Sept.) 1954.

A case of paramyotonia is described and the condition traced through four generations of the patient's family. This relatively rare and benign form of myotonia is characterized by spontaneous stiffness and occasionally paresis of muscle upon exposure to cold. The loss of function may last from minutes to hours and is relieved by warming the part. There are no pain, edema, or color changes and no characteristic constitutional symptoms. The author stresses that the condition is hereditary, transmitted by a dominant trait, and usually becomes manifest within the first few years of life. Intermittent prophylactic treatment with quinine usually produces dramatic relief from the symptoms.

JONES, Chicago.

SOME OBSERVATIONS ON THE CLOSURE OF THE ANTERIOR FONTANELLE. ROY M. ACHESON and EIRLYS JEFFERSON, Arch. Dis. Childhood **29**:196 (June) 1954.

The age of closure of the anterior fontanelle has been studied clinically in 530 children of both sexes and radiographically in 127 of these children.

In this sample the anterior fontanelle closed earlier in the male than in the female. This distinguishes fontanelle closure from skeletal maturation in which the female lead is well known.

Significant statistical correlation have been found between an early fontanelle closure and (*a*) above-average height in the female, (*b*) adverse social circumstances in the male.

KELLY, Milwaukee.

AN INFANT WITH THE MILKMANN-LOOSER SYNDROME. G. ARDOVINI and G. DE MICHELI, Lattante **25**:426 (July) 1954.

The syndrome of Milkmann-Looser may be defined as "multiple symmetrical idiopathic fractures." The condition is usually found in adults and adolescents; the present case is in an infant of 15 months with rickets; the fractures were in the two fibulae and in the two cuneiform bones; the symptoms were pain and weakness. Calcium and vitamin D therapy resulted in rapid recovery.

HIGGINS, Boston.

FISSURA STERNI CONGENITA. J. W. C. DE GROOT and J. C. HUIZENGA, Maandschr. kindergeneesk. **22**:203 (Aug.) 1954.

Congenital defect of the sternum is a rare disease. In this article a 7-week-old child is described which presents a swelling in the neck and upper part of the sternum which protruded with expiration and was sucked inwards on inspiration. Palpation of the sternum revealed a fissure of the sternum. This child showed also extensive hemangiomatosis. The ossification centers of the manubrium sterni were absent.

In 1859 the first case of this abnormality was described in Holland. Drawings from this first publication are reproduced. The embryology of the condition is extensively discussed. According to the size of the defect, a total or partial fissure may exist. If an ectopic heart is present, the child is not viable. The etiology of this condition is unknown, though mechanical pressure, lack of amniotic fluid, and abnormally large organs are mentioned. These all point toward an inhibition of development. This is unlikely, as the fusion of the original two parts of the strenum commences at the cranial end. A recent theory of the lack of development of the mesosternum gives a better explanation of the deformity. The absence of the ossification centers of the sternum might be due to developmental error of the mesosternum.

VAN CREVELD, Amsterdam.

Cutaneous Diseases; Allergy

COLORED STRIAE IN ADOLESCENT CHILDREN. WARREN R. SISSON, J. Pediat. **45**:520-530 (Nov.) 1954.

Colored striae over the gluteal region are a sign of adolescence and are probably associated with steroid activity. They occur in boys as well as girls and are not necessarily associated with obesity, although they are commonly associated with acne. These colored striae become white during the later stages of adolescence.

MACDONALD, Pittsburgh.

TREATMENT OF HEMANGIOMA OF THE SKIN IN INFANCY AND CHILDHOOD BY ROENTGEN IRRADIATION AND RADIUM. ANIS ABDULKERIM, JOSEPH A. BOYD, and ROBERT J. REEVES, Pediatrics **14**:523 (Nov.) 1954.

A group of 323 cases of hemangioma of the skin were studied, and follow-up results are given. The majority were of the cavernous and strawberry types. The classifications given are according to the relative sensitivity to irradiation. Various groups are separated depending on the type of treatment used.

The sites of predilection are the head and face. Complications are not frequent if treatment is given carefully.

FROM THE AUTHORS' SUMMARY.

HYDROCORTISONE (COMPOUND F) ACETATE OINTMENT IN ECZEMA OF INFANTS AND CHILDREN. L. R. MCCORRISTON, Canad. M. J. **70**:59-62 (Jan.) 1954.

One hundred four cases of infants with eczema were treated with 1% to 2% hydrocortisone acetate in various ointment bases. In the proper bases, improvement began in 24-48 hours, and the treatment was effective in 75% to 100% of cases. Improvement in most cases was maintained for long periods, and in 60% of cases no recurrence was noted. The author feels this to be the most effective treatment in eczema.

MCGUIGAN, Evanston, Ill.

EPIDERMOLYSIS BULLOSA. W. H. MCDANIEL, Arch. Dis. Childhood **29**:334 (Aug.) 1954.

A family showing the features of severe recessive dystrophic epidermolysis bullosa is described. Four out of the total of six children were affected. One died within two weeks of birth and another died at the age of 10 years.

KELLY, Milwaukee.

CONGENITAL POLYKERATOSIS. A. TOURAINE, Presse méd., Supp. 63, p. 1289, Sept. 29, 1954.

Among the complex group of hereditary keratoses the author suggests to isolate under the name "congenital polykeratosis" a type of polydysplasia with transmissible character, the basic structure of which shows a tendency towards hyperkeratinization of the skin and its appendages and keratinization of the mucous membranes, with usual addition of a tissue or functional hyperplasic process developing in a part or in the whole of the body.

This ectodermotic condition is connected to a hereditary chain which may appear and be conveyed to the following generations either in its complete form or in an incomplete form, even monosymptomatic, and with a great deal of clinical difference.

In addition to the hyperkeratotic process, there may be, but always accessorily, other abnormalities in consideration such as atrophy of the Malpighian body, dyskeratosis, acantholysis, thus setting up all degrees of transition with those polydysplasias which are characterized by one of these abnormalities.

FROM THE AUTHOR'S SUMMARY.

DERMATOMYOSITIS. LORE KUNKEL, Ann. pædiat. **183**:290 (Nov.) 1954.

The author reports four cases of dermatomyositis in children. Two of them died after 34 and 10 months, respectively, and in the third the illness which has been present for over two years has gone into a chronic stage with occasional exacerbations. The case was only slight and is cured. The probability of autoantibodies and their effect on the clinical picture of dermatomyositis is considered.

FROM THE AUTHOR'S SUMMARY.

TWO CASES OF ERODING PLURIORIFICIAL ECTODERMOSIS. G. MAZZEO, Lattante **25**:466 (Aug.) 1954.

Two cases are reported of young children with fever and marked erosion of the epithelium of the lips, the prepuce, and the anal orifice. The giving of antibiotics and vitamins B and C quickly relieved the conditions. The Wassermann reactions were negative. Attempts were made to find a causative virus, but without success.

HIGGINS, Boston.

THE ORAL USE OF A SOLUTION OF SODIUM SALICYLATE IN THE TREATMENT OF ECZEMA IN INFANTS. P. AVANZINI, I. BOTTINELLI, and G. SANOLLI, Minerva pediat. **6**:142 (Feb. 28) 1954.

Recent reports in the literature have claimed that corticotropin (ACTH) together with sodium salicylate has proved efficacious in the treatment of eczema in infants. Italian investigators have reported that sodium salicylate has some pharmacological action similar to that of corticotropin. On this basis, 21 infants with eczema (outpatient cases) were given conservative doses of sodium salicylate by mouth over a period of two months. Excellent therapeutic results were obtained in eight cases, fairly good results in five cases, doubtful results in six cases, and no benefit at all in two cases.

HIGGINS, Boston.

DISEASE OF WEBER-CHRISTIAN. P. BRUSA and E. GRASSO, Pediatria **61**:619 (July) 1953.

The case is reported of a girl of 21 months with high fever and painless nodules of a red-wine color over the hypochondrium and sacrum. Biopsies were made and microphotographs included in the article. The fever persisted for three months and did not respond to antibiotic therapy. The injection of cortisone led to an almost immediate lowering of the temperature to normal and a rapid disappearing of the nodules. A relapse occurred two weeks later; the injection of cortisone again resulted in quick recovery.

HIGGINS, Boston.

A CASE OF CONGENITAL LYMPHEDEMA TREATED WITH HYALURONIDASE AND CORTICOTROPIN (ACTH). G. COCOZZA, Pediatria **62**:114 (Jan.) 1954.

An 8-month-old boy with congenital lymphedema was given two 8-day periods of treatment with corticotropin (ACTH), 25 mg. daily, together with localized injections of hyaluronidase; a 10-day rest period intervened. There was a definite decrease in the circumferences of the leg and thigh following the treatment; however, the swelling of the extremities had returned when the child was seen three months later.

HIGGINS, Boston.

ON THE TREATMENT OF SEBORRHEIC DERMATITIS. JIRI LUKES, Pediat. listy **9**:222, 1954.

Seborrheic dermatitis in four infants (aged 2 to 6 months) was treated by folic acid. When the organism was saturated with vitamin C, five injections of 15 mg. every other day sufficed to cure the majority of the skin changes as well as the other manifestations, except the anemia and small residua of intertrigo. Their healing could not be influenced even by considerably prolonged administration of folic acid. If the dermatitis manifests itself only by seborrhea of the scalp and intertrigo, it does not respond to the treatment described. The relationship of seborrheic dermatitis to Leiner's desquamative erythrodermia is not always simply quantitative. In the case described (third patient), the seborrheic dermatitis remaining after the treatment of the desquamative erythrodermia with chlortetracycline (Aureomycin) cleared up following the administration of folic acid and vitamin C.

FROM THE AUTHOR'S SUMMARY.

Miscellaneous

TETRACYCLINE THERAPY. WALTER S. WOOD, GILBERT P. KIPNIS, HAROLD W. SPIES, HARRY F. DOWLING, MARK H. LEPPER, and GEORGE GEE JACKSON, A. M. A. Arch. Int. Med. **94**:351 (Sept.) 1954.

The authors give a detailed report on 153 patients treated with tetracycline and found that this antibiotic was clinically as effective as oxytetracycline and chlortetracycline in these patients. Among this group of patients were 40 with acute streptococcic infections, 24 with pertussis, 25 with pneumonia, and 16 with acute purulent meningitis. Unsatisfactory responses were observed in 8 patients. The adverse symptoms, mainly gastrointestinal, were minimal. Diarrhea was recorded in five patients and emesis in an equal number. It is concluded that tetracycline appears to be at least as potent a therapeutical weapon as its analogues.

JONES, Chicago.

AN EXPERIENCE IN THE FORMATION OF A COMMITTEE ON ACCIDENT PREVENTION IN CHILDREN. RALPH I. FRIED and WILLIAM W. HERMAN, J. A. M. A. **156**:228-230 (Sept. 18) 1954.

Accidents cause one-third of all deaths in children under 10 years of age and are one of the leading causes of morbidity. Statistical survey showed that 93% of accidents in children less than 1 year of age occurred in the home, 76% in children 1 to 5 years old, and 41% in children 6 to 14 years old—65% in boys and 35% in girls. Education and publicity programs were extended to medical society meetings, maternity classes, safety groups, parent-teacher groups, and legislative and manufacturing groups. Printed material, exhibits, the press, and radio and television programs were all used. The exact benefit, of course, could not be measured.

KIMBALL, Evanston, Ill.

AMINOPHYLLINE POISONING. VINCENT J. ROUNDS, Pediatrics **14**:528 (Nov.) 1954.

The toxic actions of aminophylline manifest themselves in three categories; first, excessive stimulation of the central nervous system; second, gastric irritation resulting in severe vomiting, and third, effects on the kidney. Six cases have been presented demonstrating all of these toxic manifestations. It is believed that alertness to these signs and symptoms in the future will prove aminophylline poisoning to be a relatively common, often serious problem. In the practise of pediatrics more caution should be exercised in using aminophylline, especially with regard to dosage.

FROM THE AUTHOR'S SUMMARY.

CROSS INFECTION IN THE NEONATAL NURSERY. KATE CAMPBELL, M. J. Australia **2**:329-331 (Aug. 28) 1954.

The best insurance against nursery infection is an adequate and well-informed nursery staff, free from infection, who practice a high level of nursery hygiene; avoidance of overcrowding, and adequate isolation facilities.

MCGUIGAN, Evanston, Ill.

THE CONTRIBUTION OF THE LABORATORY TO THE PROBLEM OF HOSPITAL INFECTION. J. W. PERRY, M. J. Australia **2**:339-340 (Aug. 28) 1954.

Proper treatment and eradication of hospital-acquired infections depend largely on the use of bacteriologic studies. Occurrence of a case of infection should be followed immediately by a ward survey to locate and eliminate the source of the infection. Cooperation between doctors, nurses, and laboratory has been shown to be very effective.

McGUIGAN, Evanston, Ill.

DOSAGE OF STREPTOMYCIN IN INFANTS AND CHILDREN. M. D. GABR, M. D. GOHAR, and A. ELVAN, J. Egyptian M. A. **37**:343-347, 1954.

Studies were undertaken to determine the dosage of dihydrostreptomycin required to maintain a serum level of 8γ per cubic centimeter in infants and children. The dose was found to vary, infants under 2 years requiring more than older children.

Doses determined as optimum were 15 mg. per kilogram of body weight every six hours for age 0-2 years and 10 mg. per kilogram of body weight every six hours for 2-12 years.

McGUIGAN, Evanston, Ill.

CLINICAL EXPERIENCES WITH "ROMILAR," A NEW SYNTHETIC COUGH REMEDY. A. HOTTINGER Schweiz. med. Wchnschr. **84**:1372 (Dec. 4) 1954.

The new drug "Romilar" was administered to 112 infants, 118 preschool children, 142 school children, and 81 adults. It was available in tablets of 10 mg. or as 1% solution. It can be given to infants and preschool children in single doses of 2 to 5 mg. once t. i. d. School children require 5 to 10 mg. t. i. d. Adolescents and adults received higher doses. A single dose may be increased to 10 mg. for infants and preschool children and to 20 mg. for school children. Only in 7 of 453 patients a slight nausea occurred and in another vertigo. With an optically pure preparation, no side-effects were noted. The drug was used in cases of pharyngitis, pseudocroup, tracheitis, bronchitis, bronchitis spastica and capillaris, asthma, bronchopneumonia, influenza with bronchitis and bronchiolitis, pertussis, "recidiv of pertussis," and measles. The drug may be combined with other cough medicines (solvents, spasmolytica, secretomotoria, secretolytica, or antihistaminica). It acts exclusively on the cough irritation center.

AMBERG, Rochester, Minn.

THE VALUE OF CORTICOTROPIN (ACTH) THERAPY IN CHILDHOOD. H. GROSS and W. SWOBODA, Wein. klin. Wchnschr. **66**:521 (July 30); 541 (Aug. 6) 1954.

A review is given of the result of corticotropin (ACTH) treatment in the Vienna University Children's Clinic, particularly in rheumatic so-called collagen diseases, nephrosis syndrome, diseases of the lymphoreticular tissue, infantile eczema, and bronchial asthma. It is emphasized that the value of the treatment becomes particularly evident in severe cases, such as acute rheumatism and status asthmaticus. The results in infantile eczema are transitory, and chorea minor is not influenced.

AMBERG, Rochester, Minn.

THE SLEEP OF THE INFANT IN A HOSPITAL ENVIRONMENT. L. ZEMAN and B. FANTOVA, Pediat. listy **9**:229, 1954.

The length of sleep was studied in 54 infants in a hospital environment. The results were compared with those of 30 healthy children in their family environment. The study of sleep was utilized for an investigation into the organization of the nursing care in a hospital environment and for the popularization of the Pavlovian principles in the case of the sick among healthy workers in departments for infants.

FROM THE AUTHORS' SUMMARY.

Books

A Methodological, Psychiatric, and Statistical Study of a Large Swedish Rural Population. By Tage Larsson and Torsten Sjogren. Price, not given. Pp. 250. Ejnar Munksgaards Forlag, Nørregade 6, Copenhagen, 1954.

This book contains the results of an important psychological investigation.

The material covers 45 years of a Swedish rural population of 25,000 and comprises 1312 cases of psychosis, severe psychopathy, low-grade oligophrenia, and suicide.

This book is the first part of a two-part report. It deals with methods and basic material, age and onset of the disease, hospitalization and mortality, morbidity risks in the general population, etc. It also gives the results of consanguinous marriages in the general population and among the parents of psychotics and oligophrenics.

The second part will deal with the results of the family investigation of morbidity risks for parents and siblings of 1028 psychotics and oligophrenic probands, and will give a clinical and genetic analysis of the material.

From the present report they predict the number of psychotic cases in 1965. The research is of interest primarily to psychiatrists.

Human Heredity. By James V. Neel, Ph.D., and William J. Schull, Ph.D. Price, $6.00. Pp. 361, with 18 illustrations. University of Chicago Press, 58th St. and Ellis Ave., Chicago 37, 1954.

This book is designed for advanced students of biology and medicine. It presents modern human genetics in detail as a distinct field of enquiry in its own right. To read and understand it in detail, a thorough grasp of mathematics, including calculus, is necessary. One may, however, get a good deal out of it without spending much time on the mathematics involved. It is a complete and authoritative work, although presented in 361 pages.

While the fundamentals of heredity are emphasized, the application to practical medicine is generously illustrated from the files of the Hereditary Clinic at the University of Michigan.

In the advice about the practical use of the facts they have found, the authors are conservative. This book is valuable as a reference and as a source book. The references are numerous and are selected carefully.

Peripheral Circulation in Man. Ciba Foundation. G. E. W. Wolstenholme and J. S. Freeman, Editors. Price, $6. Pp. 219, with 48 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6, 1954.

This is a symposium on the peripheral circulation of the blood, by 18 authorities in this field. It is presented as individual papers followed by a discussion by various members of the group. These cover the methods for studying blood flow, the changes in circulation due to exposure to cold or heat, the actions of epinephrine and norepinephrine on blood flow, the neurohistology and reflex control of the circulation, and the effects of sympathectomy, the significance of cold agglutinins, and the influence of visceral activity on the peripheral circulation.

These subjects are excellently presented, as the authors are all specialists in their fields, and the discussions are stimulating and informative. The book is very well printed, and the illustrations are well chosen. It is an interesting volume for anyone interested in this work.

Beyond the Germ Theory. By Iago Galdston. Price, $4.00. Pp. 182. Health Education Council, 10 Downing St., New York, 1954.

This book is so compact that it deserves the name "Multum in Parvo." The reader is kept on the growing fringe of medicine from the first to the last page. History is not neglected. It does not minimize the germ theory but adds to it. It deals with conditions other than germs that may cause disease and the influence of these conditions on health and happiness.

Because the germ theory is so satisfactory in explaining many diseases, it prevented for a time the discovery of the causes of some diseases, such as beriberi and scurvy, which are due not to the presence of something, but to the lack of something.

The book is divided into four parts: I. Deprivation and Stress; II. Nutritional Deprivation and Stress; III. Psychological Depression and Stress; IV. Social Deprivation and Stress. The importance and far-reaching effects of these are presented in a convincing manner

This is a book that both the well informed and the student of medicine will appreciate.

Clinical Investigations with Regard to Injury of the Central Nervous System by Birth Trauma. By Dr. med. Wilhelm H. Thiele. Price, not given. Pp. 52, with 10 illustrations. Ferdinand Enke, Hasenbergsteige 3, Stuttgart W., 1954.

The symptoms and the diagnosis of intracranial disorders as consequence of birth trauma are discussed. The value of a symptom previously described by the author, an obstetrician, is stressed particularly. It is a turbidity of the cornea which immediately after birth has the appearance of ground glass. It is not shiny and transparent. The turbidity may persist for various periods of time; usually it lasts only a few minutes. It is referred to increased pressure in the cranium. The symptom is regarded as the only certain, absolutely dependable, and extremely sensitive indication of the cerebral injury due to birth trauma. In this way it was possible to demonstrate such a lesion in 8% of 1095 live births with a weight of 2500 gm. or more. In only 1% the birth trauma could be suspected as cause of death. The mechanism of the sign is discussed as well as therapy and prophylaxis. During a period of observation extending to as much as three years, in some cases, the children developed physically and mentally within the norm. Only some forms of "neuropathic" reaction types might perhaps be related to birth trauma.

Malformation tumorales et tumeurs de l'enfant. By M. Fevre and R. Huguenin. Price, 3300 francs. Pp. 588, with 184 illustrations. Masson & Cie, 120 boulevard Saint-Germain, Paris, 6e, 1954.

The authors present a very complete study of the tumors occurring in infancy and childhood. They give much credit to their work with Professor Ombredanne and Professor Leveuf. Some of their material is from records to which they had access, but their own personal experiences in the field are remarkably wide. The pathology, pathogenesis, diagnosis, and treatment are covered in full. Particular emphasis is laid on the possibility and importance of early diagnosis.

The material is given in an orderly and interesting manner. The book may be used for reference, as the index has been compiled with care. Even one with a very limited knowledge of French would have little difficulty in profiting from the wealth of material available. The numerous illustrations are well chosen. They include pictures of patients, gross and microscopic pathology, and x-ray findings.

Elements of Pediatric Anesthesia. By C. R. Stephen, B.Sc., M.D.C.M., D.A. Price, $3.50. Pp. 100 Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1954.

"The Elements of Pediatric Anesthesia" is an excellent little book. It is well and simply written, giving the basic facts and leaving out theories and speculations.

The very first chapter deals wisely and emphatically with the importance of and the necessity for continuous adequate exchange of gases.

In every anesthesia, give the patient plenty of oxygen and get rid of the carbon dioxide, is a repeated admonition running throughout the book. Nothing is more important.

In the chapter on premedication it seems that the recommended doses of morphine as premedication are a bit low, but that is a matter of opinion.

This book is excellent all the way through and is delightful reading. In fact, it should be read through again and again by every person who is giving anesthetics to children.

George and John Armstrong of Castleton. By William J. Maloney. Price, $4. Pp. 116. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1954.

This small volume so carefully annotated represents much work on the part of the author, who unfortunately has not lived to see the product of his efforts. It is a compactly written little book with all the facts available noted, and one is struck from first to last with the severe conditions under which these two physicians worked.

While Dr. John Armstrong was well known as a poet, he was not allowed to practice medicine in London because he received his medical education in Scotland. The same might have been true of Dr. George Armstrong had he paid any attention to the laws, but he practiced among poor people, and his right to practice was never questioned.

The author calls him the father of modern pediatrics, which to a large extent he was. He opened the first pediatric hospital and clinic in the world so far as is known. It is interesting that he supported this himself to a large extent and worked largely among the poor people where the death rate in London at that time was about 50% of the children born.

As far as the results with the children were concerned, he was eminently successful, but he had to give up the clinic because of lack of support, and the evidence shows that he died in poverty and that his wife did also. There is no record of when he died or where he is buried.

This book is not only a good biography but it also gives insight into the conditions in England in the middle and latter part of the 18th century.

Health by Sickness: The Problem of Immunity. By H. J. Flechtner. Price, 14.80 marks. Pp. 352, with numerous illustrations. Econ-Verlag GMBH, Postfach 9037, Düsselodrf, 1954.

This book is devoted to the problems of the reaction of the organism to the administration of antigens of whatever derivation. The chemical aspects of the mechanisms of the reactions concerned are stressed. Throughout, military comparisons of attack and defense are emphasized rather excessively and perhaps not always very felicitously. The various aspects of immunity are discussed quite thoroughly, as are its relation to allergy and the clinical implications. The limitations of existing theories are duly considered, so that it is made clear that the riddle of immunity is not solved completely. Some omissions are unavoidable, and some attention may be paid to the Shwartzman phenomenon in further editions. The book constitutes a very palatable review of the problems of immunity.

Current Concepts in Digitalis Therapy. By Bernard Lown, M.D., and Samuel A. Levine, M.D. Price, $3.50. Pp. 164, with 21 figures and 10 tables. Little, Brown & Company, 34 Beacon St., Boston 6, 1954.

The book reviews the present data on the action and the clinical use of digitalis in heart failure. The new data accumulated in the authors' laboratories during the past three years are also reviewed.

The main purpose of this book is to emphasize the following:

1. That patients in heart failure may react differently to certain dosages of digitalis, and that overdigitalization and underdigitalization may at times be indistinguishable.
2. That the toxic threshold for various digitalis preparations is profoundly influenced by the state of the electrolytes of the body, particularly by potassium and sodium.
3. That the modern therapeutic regimen of low-salt diets, mercurials, ammonium chloride, cortisone, corticotropin (ACTH), cation exchange resins, and acetazoleamide (Diamox) oftentimes results in a low potassium and sodium content of the body, but not necessarily of the blood plasma, and this markedly lowers the toxic threshold of all digitalis preparations.
4. That paroxysmal atrial tachycardia with block is at times a definite, and until recently, unrecognized sign of digitalis intoxication.
5. The authors recommend the use of their new tolerance test to determine the patient's digitalis needs. The test consists of the intravenous use of certain amounts of acetyl strophanthin, and, according to the authors, provides the only accurate and immediate guide to digitalis dosages in critically ill patients whose clinical and electrocardiographic findings offer insufficient data to determine whether they are overdigitalized or underdigitalized.

The authors present a vast amount of experimental and clinical data, and the eminence of the authors should assure the reader of the accuracy of their statements. The bibliography is complete and carefully chosen, and this little book with so much concentrated information should be read by everyone interested in this subject.

Manual of Clinical Mycology. By Norman F. Conant, Ph..D.; David Tillerson Smith, M.D.; Roger Denio Baker, M.D.; Jasper Lamar Callaway, M.D., and Donald Stover Martin, M. D. Price $6.50. Pp. 456, with 202 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5, 1954.

This second edition of a manual which first appeared in 1944 retains the convenient small size and the presentation of each major fungous disease under these headings: definition, geographic distribution, source of infection, age, sex, race and occupational incidence, symptomatology, mycology, pathology, immunology, differential diagnosis, prognosis, and treatment. There are many illustrations of clinical lesions, x-rays, and photomicrographs. The convenient organization and large amount of information makes this a handy reference.

Nutrition Work with Children. By Lydia Jane Roberts. Edited by Ethel Austin Martin. Price, $7.50. Pp. 527, with 19 figures, 24 tables, and 35 charts. University of Chicago Press, 58th St. and Ellis Ave., Chicago 37, 1954.

This book represents a complete revision of its predecessor editions. The first was published in 1927 and the second in 1935. The original was written by Dr. Lydia J. Roberts and will be remembered as one of the foremost books in the field of nutrition of the child. The present revision was written by Mrs. Ethel Austin Martin, who was formerly an associate of Dr. Roberts as a member of the staff of the Department of Home Economics at the University of Chicago. Mrs. Martin had subsequent experience as Director of Nutrition for the National Dairy Council and as the director of a school nutrition-health program in Akron, Ohio. She has had intimate contact with the practical aspects of a school health program and with teaching materials dealing with nutrition. This is apparent throughout the text.

In the present edition, more attention is given to clinical and chemical methods of judging nutritional status, and considerable material has been added on public health nutrition and the various international organizations concerned with nutrition. A roster of agencies, organizations, and movements in the United States contributing to the nutrition of children is added. The section on nutrition education in schools is particularly valuable. The last chapter in the book deals with nutrition teaching aids in schools and community programs.

A brief list of pertinent references is given at the end of each chapter. The index is adequate.

This book is a useful contribution to the literature on nutrition. It will be found especially useful by laymen, dieticians, nutritionists, physicians, school officials, and public health personnel who are interested in nutrition of children.

Illustrated Handbook of Child Care. By Wava McCulloch, assisted by Marcella Gawronski, R. N. Price, $4. Pp. 231, with 400 illustrations. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York, 36, 1954.

This is one of the most attractive books for mothers that the reviewer has seen. It contains care of the baby in the hospital, furnishings necessary for the nursery, preparation of formulas, dressing and bathing, and recognition of sickness. For his later life, there are toilet training, choice of toys, dress, baby sitters, care and nursing of illness, and the prevention of accidents. Each of these pages is illustrated with pictures by the author, who is an accomplished artist, thus making a series of whimsical drawings that make almost compelling as well as interesting reading.

These illustrations have been checked by Dr. Arthur H. Parmelee Sr. for accuracy in accepted practice, and there is nowhere the slightest pretension of supplanting the physician. This is the book the busy pediatrician can safely suggest to the mothers of his patients. It will save him countless hours of explanation, yet in no way detract in any way from his own ideas. The reviewer is only sorry that this volume was not available when he was in active practice.

A Dynamic Psychopathology of Childhood. By Lauretta Bender, M.D. Price, $7.50. Pp. 275. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1954.

This volume by Lauretta Bender and various collaborators is a collection of various publications from the children's service of the psychiatric division of the Bellevue Hospital, in New York City. It constitutes the third in a series of volumes from this service. As is usually the case in collections of papers, there is considerable unevenness in the character of the various chapters, which cover such varied subjects as the psychology of the development of language and the symbol, hallucinations in children, imaginary companions, internalization of fantasy objects in the development of children, impulsions, compulsions and obsessions, sexual expression of identification conflicts, children's reaction to death in the family, psychoanalytic remarks on "Alice in Wonderland" and Lewis Carroll, comic books and the ideology of children, and children's reactions to war. Fortunately these papers have been revised editorially and brought up to date.

The richness of the clinical material of the children's service of the psychiatric division at Bellevue Hospital is abundantly evident in the book. Clinical examples are employed to good advantage throughout and serve to render greater clarity to the text. The literature is reviewed adequately to enhance the utility of the volume as a reference. A doctrinaire approach is avoided, and interpretations are based upon appropriate clinical experiences.

For the pediatrician some chapters (like that on the "Psychology of the Development of Language and the Symbol" and "Psychoanalytic Remarks on Alice in Wonderland and Lewis Carroll") may be somewhat abstruse. Others, however, such as "Imaginary Companions" and "Children's Reactions to Death in the Family," may be very helpful to the physician desiring to delve more deeply into the psychological problems of children. This book, therefore, would be considered a reference volume for the pediatrician, although it should be part of any library in child psychiatry.

Diagnostico y tratamiento de la deshididracion en el lactante. Ponencia al IX Congresso nacional de pediatria. By E. Jaso Roldan and E. de Yturriaga. Price, not given. Pp. 220, with 130 illustrations. Instituto español de hematologia y hemoterapia, Madrid, 1954.

This very excellent symposium written in Spanish was initiated from discussions at the National Congress of Pediatrics. It consists of three parts, the first deals with the physiology and metabolism of dehydration and fluid balance. The second part discusses the diagnostic problems involved, and the last part deals with the various forms of therapy. This is very fully discussed, including various solutions and their physiological actions. The charts are excellent, and there is a very complete biography. This makes excellent reading for anyone interested in the subject.

A Thousand Families in Newcastle upon Tyne. By James Spence, W. S. Walton, F. J. W. Miller, and S. D. M. Court. Price, $3. Pp. 210. Oxford University Press, 114 Fifth Ave., New York 11, 1954.

This important compact book is a real contribution to the knowledge of health and illness during the first year of life. It is the result of a survey planned by the late Sir James Spence, first holder of the Nuffield Chair of Child Health, in the University of Durham.

An intensive study was made of all children born in Newcastle upon Tyne during the months of May and June, 1947. The number of babies was 1142. It is planned to continue the study for at least seven years.

The study was a highly cooperative affair. The medical men were furnished by the University Health Department; the nurses and secretarial staff by the Public Health Department. All worked in cooperation and with the advice of a professor of social medicine and a professor of economics. The family doctor of the patients worked with them. Photographers and others who might add to the success of the work were available.

All sources that might help the study were used, and all circumstances that could influence the health of the children were considered. Each child was visited at least seven or eight times during the year. As an example of the detail used, we might cite the observation that the earilest date that the child was taken out was a case taken to the cinema on the ninth day of life.

During the first year there were 1400 infective illnesses that required precision in diagnosis and treatment, but few of such cases are presented in teaching hospitals. On the other hand there were 18 cases such as intussusception, meningitis, and osteitis, which are the classical material for teaching.

The results of the first year of the survey give much that is valuable in preventive medicine, treatment, and medical education. Incidentally, the study shows that pediatrics per see is enough to tax the ability of any one person.

The atmosphere of the book is one of help, not criticism. Future reports are awaited with interest.

Herzkrankheiten im Säuglingsalter. By Priv. Doz. Dr. Ettore Rossi. Price, 60 marks. Pp. 373, with 8369 illustrations and 14 tables. Georg Thieme Verlag, Stuttgart, Herdiveg 63, 1954.

This new treatise on "Herzkrankheiten im Säuglingsalter" is the first systematic presentation of all forms of heart disease in infancy in a book form. Written by Priv. Doz. Dr. Ettore Rossi, who is Chief of the Pediatric Cardiology Division at Prof. Guido Fanconi's well-known Children's Hospital of Zurich, Switzerland, this book is highly recommended to all pediatricians, internists, radiologists, and other physicians who are interested in the diagnosis and treatment of heart disease in infancy.

The author divides the book into five chapters: Chapter I—"The Normal Heart in Infancy"; Chapter II—"Congenital Malformations of the Heart"; Chapter III—"Heart Disease in Infancy

Not Due to Congenital Malformations"; Chapter IV—"Heart Involvement due to Extracardiac Factors," and Chapter V—"Treatment of Cardiac Decompensation in Infancy."

Each entity is clearly described from the standpoints of the hemodynamics, clinical findings, roentgen ray, electrocardiography, angiocardiography, and catheterization of the heart and of the great vessels. In addition, the differential diagnosis, therapy, and a brief summary of each entity is also included. The various forms of the acquired and of the congenital malformations of the heart are illustrated with the authors' own case reports. One hundred sixty-five separate case reports are included. The bibliography of the world literature up to 1954 is extensive, the data are up to date in almost all chapters and reflect the rapid development of our knowledge of this subject. The book is well organized, well written, and should be in the library of every physician interested in heart disease in infancy.

Tuberculosis in Childhood and Adolescence with Special References to the Pulmonary Forms of the Disease. By F. J. Bentley, S. Grzybowski, and B. Benjamin. Price, $5; 30 shillings. Pp. 259, with 67 radiographs. National Association for Prevention of Tuberculosis, Tavistock House North, Tavistock Sq., London W. C. 1, 1954.

This is a very thought-provoking and interesting report of the authors' experiences in the treatment of tuberculous children at High Wood Hospital, near London. It should prove of great value to the pediatrician interested in tuberculosis because it discusses so many phases of tuberculous disease in children. The great variety of clinical material, the long period of observation in the hospital, and the excellent follow-up (over 90%) make this report outstanding to those interested in the diagnosis and prognosis of tuberculosis in children. To obtain a complete picture of this protean disease in children, it is necessary to study reports from many sources, since the clinical material will vary with the type of hospital. The cases from High Wood include many examples of uncomplicated primary tuberculosis and of forms of tuberculosis such as endobronchial lesions and segmental obstruction which commonly occur during the first six months of the disease but are rarely fatal. There is a very good chapter on pleurisy with effusion—a late complication of primary tuberculosis—and an excellent discussion of a number of cases of chronic pulmonary tuberculosis. Relatively few cases of miliary tuberculosis and meningitis are presented, probably because these cases usually develop early in the course of primary tuberculosis and are seen, therefore, in a general hospital and not in a hospital specializing in tuberculosis. This book deserves careful study by pediatricians.

Treatment of Acute Poliomyelitis. Edition 2. By William A. Spencer, M.D. Price, $3.75. Pp. 134. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave. Springfield, Ill., 1954.

This is essentially a loose-leaf notebook with an outline of treatment of a series of selected problems in the care of patients with respiratory failure in poliomyelitis. Each subject is handled first by a boxed-in list of tabulated important points, and this tabulation is followed by one or two paragraphs of discussion.

The book is planned to furnish a quick reference manual for the busy practitioner who is faced, for the first time, with such problems. Attempts to furnish material so that he who runs can read, must suffer from the limitations of great briefness by the necessity for dogmatic statements and for outlines instead of discussions. All these lead to certain inaccuracies and a temptation for routinization of treatment which may act as a protection for the patient in the hands of a practitioner with excellent judgment, but might do harm if literally and uncritically accepted.

As a whole, the notes are presented with precision in clear-cut statements that would be accepted by most students of this general problem in poliomyelitis. Objections would be mostly to details about which discussion might reveal only differences of opinion, but there are other places where inaccuracy occurs. These items cannot be detailed. As an example of the tendency toward too great routinization is a table which lists the suggested settings for a tank respirator for patients of different ages, giving one pressure for a child under 2 years, another one for a child between 5 and 10 years, etc., with such slight differences of pressure that one can wonder at its justification, particularly as there seems to be no physiological basis for such exactness in directions. The whole problem of the indications for tracheotomy, a most confusing problem, is handled in one page, although, indeed, discussions of facets of the problems can be found on other pages. In certain parts of the manual attempts are made to discuss the very great problems of poliomyelitis, such as causes of muscular weakness in this disease, in brief and unsupported statements where the intranuncial nerve cells of the spinal cord are specifically blamed. One

would doubt that knowledge has progressed to the point where such exactness of statement is justified. Certain statements are made that we doubt the authors themselves would accept, such as "respiratory muscle paralysis is the most common serious complication of poliomyelitis." Although it is not important, one could question whether this is really true, whether disturbances of the nerve centers in the brain are not commoner, as well as more serious.

The danger of such a book is that it would be accepted by a student of disease with contentment as being a complete treatise on the subject. As a whole, it can be said that this manual will be useful and presents a device for quick reference, for which there is at present no adequate substitute.

How to Get Along with Children. By Frank Howard Richardson. Price, $2.95. Pp. 172. Tupper & Love, Inc., 1090 Capitol Ave., Atlanta 2, 1954.

Dr. Richardson is an author of recognized stature in the field of child behavior, especially in the adolescent age group. In this book he attempts to cover the entire age span from birth through adolescense. His aim is laudable, and his approach is on an admirable common-sense basis. However, his treatment is perhaps too sketchy and in many places could have been greatly expanded, to the benefit of the reader.

The technique of asking a question and then answering it is sometimes good, but when for every question asked there are scores which might equally well have been included, and when the answers are of a length more suitable to a newspaper column than to a supposedly more comprehensive book, the use of this technique is not as successful as it might be. Also, in answer to questions about sex the author of successful books on this subject for adolescents should not merely advise the reader to read a book by another author.

In summary, the approach to the lay problem of child behavior is good. The book is good so far as it goes, but many parents will wish there had been more discussion than is included here on many problems.

A Primer of Pulmonary Function. By Harold Guyon Trimble, M.D., and James Kieran, M.D. Price, not given. Pp. 22. California Tuberculosis and Health Association, Oakland, Calif., 1954.

This is a concise, authoritative, and significant contribution to the field of pulmonary physiology. The subject matter is an up-to-date presentation of pulmonary function tests. It is valuable to the surgeon and medical man alike in that from the application of these tests one can not only determine the patient's present pulmonary status but also what can be anticipated in the course of his disease or postoperatively.

Cystic Fibrosis of the Pancreas in Infants and Children. By Dr. Charles D. May. Price, $3. Pp. 93, with 16 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1954.

This is a monograph in the American Lecture Series. It is short and concise but comprehensive in its clinical approach. There is a short history of the disease. The physiology of the pancreatic and pulmonary lesions is accompanied by excellent illustrations. Then follows a well-organized discussion of the clinical manifestations, diagnosis, and treatment. Unfortunately, recent studies such as those on the composition of sweat are not included.

This small book is beautifully printed and bound. It is 93 pages in length and contains 16 illustrations and 83 references.

CORRECTION

In the article by Drs. Randolph Batson, John Shapiro, Amos Christie, and H. D. Riley Jr., published in the September, 1955, issue of the A. M. A. AMERICAN JOURNAL OF DISEASES OF CHILDREN, page 323, the second sentence in the first column should be read as follows: The latter is the least common of this group, approximately 41 cases having been reported since Letterer's[1] report in 1924.

In Case 13, page 333, the sidehead "Biopsy of Skin" should read "Biopsy of Lymph Node." In the "Comment" on this case the word "Skin" should be omitted.

In Table 1, the column head "Autopsy Pathological" should read "Autopsy Confirmation."

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1. Editorial: J.A.M.A. *134*:606 (June 14) 1947. 2. Hansen, A. E., and Burr, G. O.: J.A.M.A. *132*:855 (Dec. 7) 1946. 3. Hansen, A. E.; Knott, E. M.; Wiese, H. F.; Shaperman, E., and McQuarrie, I.: Am. J. Dis. Child. *73*:1 (Jan.) 1947. 4. Hansen, A. E.: In, Vitamin B_6 in Human Nutrition, Report of the Tenth M & R Pediatric Research Conference, Columbus, M & R Laboratories, 1954, p. 51. 5. National Research Council: Maternal Nutrition and Child Health, Bull. 123 (Nov.) 1950. 6. Meyer, H. F.: Essentials of Infant Feeding for Physicians, Springfield, Illinois, Charles C. Thomas, 1952, p. 44. 7. Martin, C. W.: New York State J. Med. *32*:1012 (Sept.) 1932. 8. Stoesser, A. V., and Nelson, L. S.: Journal Lancet *73*:487 (Dec.) 1953.

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*Shwachman, H., Children's Hospital, Boston, The Child in Health and Disease, Grulee and Eley, 2nd Edit.

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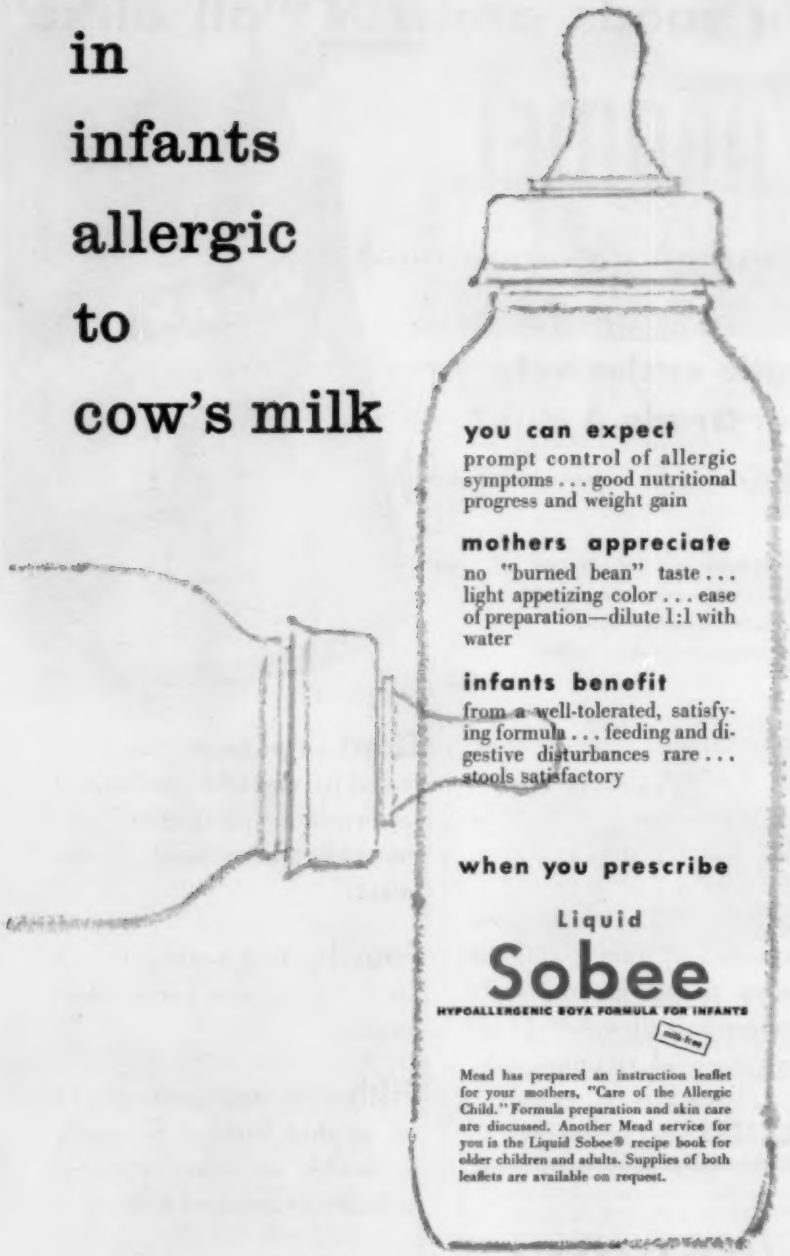

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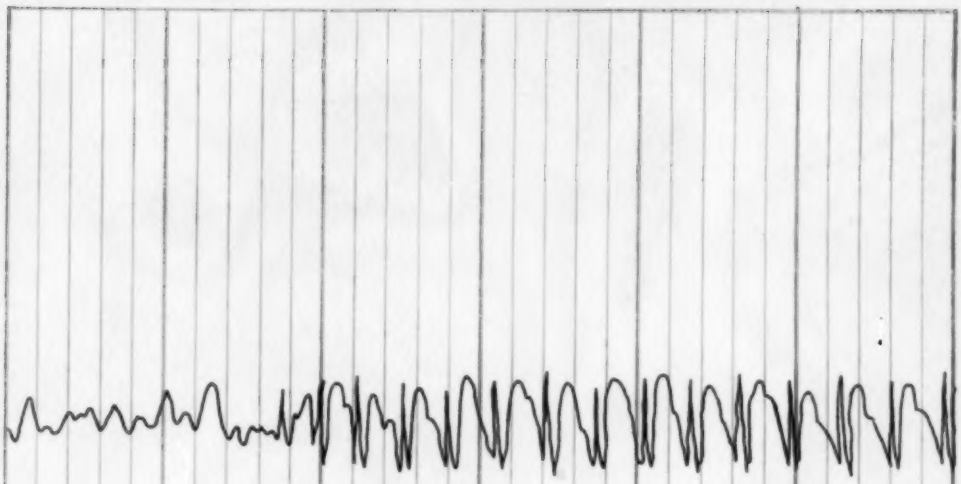

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